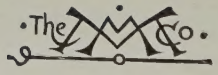
A SYSTEM OF MEDICINE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A

SYSTEM OF MEDICINE

BY MANY WRITERS

EDITED BY

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VOLUME I

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TO

SIR J. RUSSELL REYNOLDS, BART., M.D., F.R.S.

PRESIDENT OF THE ROYAL COLLEGE OF PHYSICIANS

THIS WORK IS DEDICATED

IN MEMORY OF THIRTY YEARS OF FRIENDSHIP

BY THE EDITOR

PREFACE

The latterday Editor of a *System of Medicine* is met on the threshold by a vast increase of the matter with which he has to deal. In the Introduction some fuller reference is made to this increase; at present it is sufficient to point out that to ætiology alone the whole chapter of bacteriology has been added. Contributors speak of the difficulty of keeping the matter within anything like the limits assigned to them; for what is true of ætiology is true more or less for every section of every chapter.

When nothing more than opinions were needed as support for opinions teaching was easily made dogmatic and compact. In modern Medicine, however, every statement must not only be submitted to verification, but submitted again and again. The methods of verification must also be punctually given, and all statements as accurately reported as if for cross-examining counsel. We cannot be any longer content to state that "the soldier said" such and such a thing, but we must give our testimony at first hand, or from carefully accredited and recent sources.

Again, pathology has not only become intolerant of second hand evidence, but is irresistibly leading us to the study of *origins*— to the study of processes in a disinterested way as an aspect of natural history. It is impressed upon us in the field of Medicine, as in all other fields of knowledge, that to pursue knowledge with a consciously utilitarian end before us is to fail even in our immediate ends. It is as true now as it was two thousand years ago that Wisdom must be sought with a single heart devoted to her love and service;

and that even the relief of humanity cannot stand always first in our sight.[1] The ultimate use of thought, no doubt, is to guide our conduct; but biology must be studied as an end in itself before we can hope to apply biology successfully in the conduct of living processes.

On the other hand, were an Editor to rule out of his treatises all formulated thought on things not measured or comprehended he would err in the opposite direction. To speak or act as if things seen imperfectly or confusedly do not exist were worse than pedantry; all that lore which has the approximate truth of a large number of observations — of a number large enough to reduce the margin of error, if not to expel it, — would be rejected, and with it much useful art. Many a bridge was built before engineers learnt to calculate stress; and although traditional medical lore may prescribe for evils wastefully, yet in a more or less cumbrous or roundabout fashion it often attains or approaches the desired purpose. In a strange land a tedious, painful and circuitous route is better than no route at all. It has been our endeavour to preserve these traditional practices and these hazy views, where we cannot replace them by more definite measurements, lest we pull up wheat with tares, and, waiting for more light deprive sufferers meanwhile of some kind of aid however rude.[2] The acquired tact and patient study of individual physicians, as I have indicated under the head of Prognosis in the Introduction, must pilot them through these uncharted waters.

It has been my duty to consider in what way the large mass of new matter may be accepted without an enormous expansion of the limits of this work. Contributors have done their best to be concise, and have not in any instance resented editorial co-operation to this end. Footnotes as a rule have been excluded, and references in the text have been replaced by very select "bibliographies."

Perhaps all "overlapping" parts ought to have been ruthlessly

[1] "That knowledge may not be as a curtesan, for pleasure and vanity only, or as a bondwoman, to acquire and gain to her master's use; but as a spouse, for generation, fruit, and comfort." — *Adv. of L.*, lib. i.

[2] No better examples could be given to illustrate this argument than the revival of counter-irritation and of bleeding on reasonable grounds and discriminating methods.

excised, but I have often held my hand; and this for several reasons. Continual cross-references tease the reader; the same matter may take on different meanings with changes in its context, and various writers may put the same substance in very different lights. For example, the repetitions involved in Sir Joseph Fayrer's review of "Fevers" from the stand-point of an Indian physician have been accepted; and I am bold to think that my readers will thank me, even at the cost of some additional pages, for presenting to them the uncurtailed opinions of this distinguished member of our profession, particularly those of them who practise in this vast possession of the Empire. To have given cross-references to the respective specific fevers at every division of so important a chapter would neither have been fair to the writer nor tolerable by the reader.

Historical matter has been for the most part omitted: this relieved the *System* of some burden, and at little loss to the reader. During nearly two millenniums of time and over broad domains of the world the story of Medicine has been but a melancholy study. To the curious scholar the "pseud-ideas" of sophists, the dreams of mystics, the quaint conceits of monkish craft, the devices of magicians, the grotesque or brutal records of folk-lore may be entertaining, or even instructive; far be it from us to find any human things alien. *Primus sapientiæ gradus est falsa intelligere.* Here may be some felicity of observation; there some shrewdness of opinion: yet after all we read the history of medicine rather for the honour of a certain few of our ancestors than for our own instruction. To enter into this subject fully would occupy much of the very pages which I am trying to economise; but I may briefly say that the only period of the past history of our profession which can interest the medical student directly is the Medicine of Ancient Greece, which came to life again on contact with our own. Greek medicine of the fifth century B.C. seems to be almost of yesterday; English medicine of the twelfth century of our era seems more alien to our thought than the Galenical treatises of the Arabs, and almost as grotesque as the demonology of the Chaldeans. No modern book of Chemistry

deals with the stories of Alchemy, nor of Astronomy with those of Astrology.

The great profession of the Law may feel a just pride in the growth of its reasonable and gradual dominion; Medicine, after the decay of the school of Hippocrates, and in countries which knew not that master, became the tool of priests, slaves, charlatans, or literary men. To trace the living waters of the healing art and the auxiliary sciences in their secret channels under the foundations of the Temple, of the Gymnasium, of the Museum, or of the Marketplace, until they burst forth once more in the time of Vesalius, of Harvey, of Morgagni, of Haller, of Hunter, of Bichat, of Bernard, of Laennec, is not a pursuit for these pages.

The Prolegomena which open this volume, and others which will appear occasionally hereafter, are in part to enlarge the conceptions of the student, to lead him to see the domains of Medicine from points of advantage: in part, by means of these broader surveys of General Pathology, of Statistics, or of Dietetics and Therapeutics, to avoid some repetitions, otherwise necessarily frequent, in the several articles of the work.

The pleasant duty remains of thanking my contributors for the kindliness, good faith, and intelligent support which they have manifested throughout this undertaking, which, although now published in small part, is in a fair way of completion. If all be as well as the promise of it the future volumes will be published without long delay. The first volume of such a co-operative work is the most arduous: the time allotted to the several contributors is shorter than to those whose treatises come in later. Moreover, the heavy sickness of the two past winters played havoc with my staff. Some of these, prostrated with one plague or another, have striven hard on their imperfect convalescence to perform their task. Others, such as the late Dr. Sturges, Dr. Beaven Rake, and Prof. Walley, had finished their work, but not for us. My cordial thanks are due to Dr. Cheadle, to Dr. Phineas Abraham, and to Dr. M'Fadyean, for generously taking up the labours of those who had passed away. Professor Burdon-Sanderson took up the chapter on Fever at very short notice, and wrote it under severe pressure of time and other engage-

ments. Dr. Rolleston has given me invaluable aid throughout in the reading of proofs, in advising me continually, in forwarding my arrangements with contributors in London, and in many other ways.

Finally, I have to thank those kind and able friends who have not only given me the advantage of their articles on special subjects, but have spent much time and pains, which they could ill spare, in the arrangement of certain sections of the System or in proof reading. Invaluable help of this kind has been ungrudgingly given to me by Dr. Ferrier (Cerebral Diseases), Dr. Manson (Tropical Diseases), Dr. Payne (Skin Diseases), Dr. Savage (Mental Diseases), and Dr. Felix Semon (Laryngeal Diseases). Dr. Venn and Mr. Thomas Marshall, of Leeds, have given me valuable help in the revision of the Introduction, for the contents of which, however, I am wholly responsible.

T. C. A.

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INTRODUCTION

Medicine as a System. — The title which has been chosen for this work is one which may be necessary for present purposes, but one which on logical grounds cannot be defended: a System of Medicine cannot now be written, either by one man or by many, and this state of things is by no means to be regretted. Of a body of empirical knowledge a system may be made, and in such a system place may be found for new accretions or elaborations; before the days of Bacon, for example, and even after the publication of the *Novum Organon*, it was the ambition of learned men to attain to encyclopædic knowledge, to spread themselves over the whole realm of it, and laboriously to gather all its products into a Corpus or System: this was their end. To construct such an "Orbis Doctrinæ" seemed to them to be a mere matter of time, ability and capacity; and to its attainment many noble lives were devoted. It seems probable that even Bacon himself had little idea of the remote consequences of his own method: it seems probable that he believed the new Organon to be a key to the discovery of natural knowledge which at no distant time would reveal that realm to us as a band of scouts, armed with other weapons, might reveal to us, let us say, the parts of Central Africa. A system of natural knowledge would thus have completed the encyclopædia — the "Institutio in circulo" — already fairly sufficient for the student of discovered subjects such as theology and philosophy. That his method, as afterwards interpreted and extended by Newton and later thinkers, had an application correlative in depth and extent with the perceptible universe, and that, this depth and extent being infinite in all dimensions, its analysis must be inexhaustible, Bacon perhaps never apprehended.[1] The complexity and the infinity of nature were not and could not be realised in the infancy of the investigation of it. As later generations learned that natural knowledge cannot be held in categories, but must be conceived as a classi-

[1] Glanvil (*Vanity of Dogmatising*) says: "And 'tis the observation of the noble St. Alban, that philosophy is built upon a few vulgar experiments." The noble St. Alban thought more wisely than this, but not altogether out of this fashion. In saying this I do not forget the well-known 127th Aph. of *N. O.*, lib. i. My view is founded upon Bacon's own way of going about to apply his method, which indeed he drew almost entirely from Aristotle.

fication by kinds[1] whose similarities and dissimilarities are inexhaustible, it became obvious that a system uniform in its proportions and parts is impossible; or that, so far as possible, such a system would indicate not progress, but arrest of development — in a word, a stereotype.

In times when knowledge is almost stationary, as was approximately the case, for instance, in the Arabian schools, a System of Medicine may be thus made; its parts will be classified by means of resemblances only as deep as the foundations of contemporary knowledge: thus, for example, a specious group or class of pulmonary diseases may be made. At no time, however, is knowledge quite stationary; and, even at its most stable moments, some deeper resemblances, truer explanations that is, are hit upon by this man or the other, and the fixity of the system and of its categories is disturbed. On the revelation of profounder resemblances objects hitherto set near each other are detached, and objects far apart in the system are approximated. Thus, in respect of the pulmonary diseases, kinds of pulmonary phthisis or of pneumonia may be carried away to the class of Infectious Diseases, and so forth; every new explanation bringing about a change of the order.

Moreover, in seeking and verifying explanations, we find that pioneers in natural researches do not rule themselves as an army in the field, pressing forward on a uniform plan and upon all faces of the enemy at once; but attacks are made upon certain quarters, and individuals or companies penetrate particular parts regardless of the advance of others. At one time morbid anatomy, at another bacteriology, at another pharmacology, or several quarters of each of these respectively, are the chief subjects of inquiry; progress in one direction thus passes out of immediate relation to progress in another. Individual tastes, again, occasional facilities, and the advances of ancillary sciences or arts, modify the rates of progress in the several sections of each department of natural knowledge. It is then characteristic of natural knowledge, if not strictly pertinent to it, that its progress should be largely unsystematic; although from time to time generalisations are made, such as the classification by genetic affinities, which break up older systems, and bring some method into large groups of things which before had appeared to be unrelated. Thus no doubt, as generations of men pass, the subjects of knowledge are more and more co-ordinated; but, if progress continue, we shall observe still that new and irregular adits are driven into the unknown before the older winnings are completely surveyed and classified.

The reader will, therefore, be disappointed if, on opening the following pages, he expects to find a System of Medicine formally so called:

[1] The logician may remind me that to put matter in natural groups and to classify it are the same thing; and that as "natural groups" do not exist, such a classification, like any other, is but a convenient device for a particular purpose, a way of looking at things from a certain point of view. In the biological sciences, however, classification, since it has become an expression of affinities, — that is, since the publication of the *Origin of Species*, — has taken a larger meaning, and is a conceptional summary of permanent and universal convenience.

he will rather find our knowledge set forth on the whole as immediate convenience and the exigencies of contemporary learning may dictate. The arrangement which may seem good to one editor may be displeasing to another: in biological subjects all editors desire to place their matter in groups as natural as possible — to classify its parts by the tie of kind, so that the classification may become explanatory of the matter; on the other hand, orders of convenience are no less imperative, and a treatise of Medicine must be based upon a compromise. If herein the formal mind occasionally feel pain, I trust it will be remembered, as I have said, that irregular expansions which burst the limits of a "System" are signs of life and progress.

Some endeavour I have made to recompose my matter in accordance with the latest advances of science; yet when faced on one side by a large block of ignorance, or diverted on another by some dictate of convenience, I have not hesitated to regard rather the habit and convenience of the ordinary reader than the doctrines of the systematic thinker: I have endeavoured to make provisions for the former and for the latter necessities, yet, systematising where I can, and "distributing our ignorance" as equally as I can, I have had to present much of the matter in the unconnected way in which it was discovered.

Science and Practice. — No thoughtful man versed in the methods of natural inquiry can fail to be reminded at every moment of the ultimate and universal dependence of every one group of phenomena upon every other. Too often we regard causation as a pedigree drawn up on the plan of primogeniture in the male line — as a series of linear sequences, each result owning a parent, and so on until a primal cause is reached. I need not say that such a conception, and the use of such metaphors as "the chain of causation," are so narrow as to be false. So incalculable are the properties of things, so contingent is each event upon every other, that anything like a final presentment of causation is impossible, nay, inconceivable by our limited faculties; and our propositions are but provisional formulæ which, if permitted to harden into aphorisms, become fetters of thought. Our formulæ, then, should be in a state of continual flux: fresh exceptions are continually turning up, and fresh qualifications are incessantly made. On the other hand, without provisional formulæ we cannot act, and in action lie the purpose and end of medical studies. The "merely scientific" physician is apt to be blind to useful manœuvres which rest rather upon the accidental than upon the more permanent qualities of things: indeed, the practical man often sees more of the surface of things than does the analytical man, and thus keeps more sense of proportion, more of the sense called "common." So it comes about that in practice personal tact and character are as important to the operations of a physician as scientific equipment. He has to deal with men of limited vision, full of accidental qualities, and subject to accidental disturbances; and the tact which deals with these confused and conflicting attributes is born rather of a wide survey of the outsides of things, and of transitory conventions, than of a penetrating insight

into causation. Excessive concentration, if it fit a man for analytical study, may unfit him for the world. Moreover, the purely scientific physician tends to undervalue opinion, as the man of the world to overvalue it. Now, prevalent opinions, though not formal truth, generally contain truth, and this the practical physician does not fail to perceive; nor does he forget that the observations of any one person, however profound, being the observations of an individual of brief life and limited faculties, need some tempering by traditional lore — by the embodied opinions of a vast number of observers over a long period of time; opinions which, individually inaccurate as they may be, yet make collectively an approximation to truth of no small value to the man, be he statesman or physician, who has usually "to act on a choice of second best courses" [*vide* paragraphs on Prognosis].

Methods. — We are met at the outset of our study by the questions — *What is health; and what is disease?* The man who lives to the age of a hundred years, and who during that time suffers no pain, and is continually able to make use of the powers proper to his age, would by universal testimony be regarded as an example of health: yet even the life of such an one would not always be at its best; and health, like every other such name, is to be used in a relative sense. Into the life of the healthiest man disorder must frequently enter. Absolute health is an ideal conception, as the line of the mathematician, the ether of the physicist, and the atom of the chemist; it is a positive conception of a perfect balance of the moving equilibrium which we call systemic life: disease is a negative conception, and signifies something less than this perfect balance.

In other times, nay, even in our own, there has been a disposition to regard disease as something imported into the system, as a possession of it by a malign agent which may be expelled by some sorcery or virtuous herb; in this sense health and disease are not different attitudes of one thing, but a binary combination. Insensibly this personification of disease falls by a sort of refinement into the "principle" of the vitalists, as in the phrase of a distinguished physician who describes a patient as "saturated with insanity"; or it becomes the peccant humour of a less unscientific pathology; or, again, it may be identified with a microbe or a virus. Yet to speak thus is to confound disease with the causes of disease, and to use figurative language to our confusion — the "perilous stuff" from which the bosom must be cleansed is no more a disease than a blackthorn staff is a broken head. The blackthorn may be the cause of a green wound; by this gate other bacilli, less gross in kind, may enter the body, and cause the oscillations in its system which we call fever; the consequent dislocations and disturbances in the body are properly called diseases. A cancer is no more a disease than the hyssop on the wall: a cause of disease it may be, but the disease is in the damaged tissues, which are irritated, invaded, or choked by the growth.

Again, whether the causes be prevented inside the body or outside it,

are matters of no essential difference. To kill Laveran's microbe[1] within the body by eating quinine is not to cure an ague, but to prevent the cause of a future ague: the ague itself is a perturbation of the systemic balance which will usually yield to the *vis medicatrix naturæ;* that is to say, to the tendency of all stable equilibriums to maintain themselves — the *vis medicatrix naturæ* being an aspect of inertia.

If we keep clearly before us this distinction between the causes of disease and disease itself, we shall use our remedies more intelligently; we shall see how dominant is the sphere of preventive medicine, and that curative medicine is often but the ancillary mouse which liberates the body for its own work of recovery.

To know disease, then, we must first know the latitudes of health; we must study the balance of forces in their normal play before we can comprehend and neutralise the disturbances to which this balance is subject. The corporeal system of man is one of vast multiplication and differentiation of members; in him, therefore, comprehension of the system is most difficult. As we descend the scale of life, and study simpler systems and simpler functions, description becomes easier; and physiologists, building up our knowledge of the normal by the comparative method, take pathologists with them, who, in their turn, working upwards from the lowest forms of life, or the embryos of the higher or the embryonic tissues of the higher, are revealing to us day by day the secret ways of the earliest and simplest deviations from the normal — that is to say, the elements of disease [*vide* arts. on "Inflammation," "Fever," and "Pathology of Infection" in this volume]. Again, as the building up of an organism is not by permanent accretion like the building of a house, but by an incessant repair of decay, the student of the normal, that is the physiologist, is constantly in the presence of pathological features. As the healthy, so the normal is but a relative term; that which is normal in one series may be abnormal in another, and thus the physiologist and the pathologist are intimately one: physiology as well as pathology is concerned with decay. The comparative method necessarily embraces the work of both, pathology being one aspect of physiology; to speak metaphorically, it is the reverse view of physiology, the study of accelerated or irregular rates of decay. Disease is a matter of time relations.

What, then, is the nosologist? The nosologist bears the relation to the pathologist that the naturalist or morphologist does to the physiologist; as the pathologist classifies the morbid variations of plants and animals, so the nosologist describes the natural history of diseases: the nosologist, as such, has no concern with curative means; he has his views of the balance of forces, but has no concern in the promotion of them. Cure is an art; it is the application of these sciences, and is the concern of the physician: a physician is an engineer who cannot construct, but is skilled in conservation and repair.

Classification. — The nosologist or clinician, describing and comparing

[1] The use of the word "microbe" is not to be limited to bacteria. A general term for minute living things is required, and "micro-organism" is too cumbrous.

organisms which have deviated from the normal balance of function, finds that, infinite as are the gradations between health and disease and between one mode of perturbation and another, yet these perturbations tend to resolve themselves in certain ways, to fall into certain morphological groups which present some low degrees of constancy. By these recurrent characters he is enabled to classify them; and this he tries to do after the method of a naturalist, that is, on an explanatory arrangement based upon degrees of genetic affinity. As the naturalist cannot, however, go far without the anatomist, so the nosologist, soon finding that a study of superficial features leads to classifications which, however convenient for the time, are but provisional, has to classify by likenesses of a deeper and a deeper kind; and as he does so he becomes a pathologist. As the naturalist without the help of the comparative anatomist might classify, let us say, the swift with the swallow, so the nosologist without the comparative pathologist might, as he has done, classify leprosy with psoriasis, tubercular with typhoid enteritis, sarcoma with carcinoma, and so forth.

Here, however, we are led to the reflexion that to regard and name diseases as species, or even as varieties, in a biological sense, is an error of the same kind as to regard them as entities. A disease is a particular state of an individual; and, although certain families show persistent bents to certain kinds of morbid variation, yet the constancy of this fashion bears a very small proportion to that of the characters of a variety in a biological sense. Moreover, although careless clinical teachers will continue to speak of the "development" of this or that disease, yet disease is no new advance, but a retreat, a stage of decline failing in relative stability, a state which must end either in a recovery of the normal balance or in dissolution. All attempts to describe diseases in terms equivalent to the genera, species, or natural varieties of plants or animals are then erroneous; they lead to mistakes both of theory and of practice, and to ignorance of the underlying unity in the various forms of disease. A sick plant or animal is but itself in another state, a state more transient and less useful.

On the other hand, amid the instabilities and the frequent and rapid changes of natural perturbation, nosologists in early times — times earlier than our records — observed, nevertheless, that symptoms do not occur haphazard, or congregate pell-mell, but that they tend to arrange themselves in recurrent groups of some likeness, so that a medical morphology is possible. We should anticipate perhaps that, inasmuch as in animals of the same kind the several systems of the body are approximately alike, so their disorders, like autumn leaves, would appear with fairly uniform features within the kind. We do find, accordingly, in man that diseases, or symptom groups, present broad features of resemblance, diversified in subordinate detail as individuals are diverse. No two men are alike at all points, and no two cases of disease are identical; but comparative nosologists tell us that, so far as observation has gone, each kind of plant and each kind of animal seems on the whole

to have certain sets of morbid characters more or less peculiar to itself.

That symptoms do not occur in disorderly jumbles, but tend to form groups of certain degrees of constancy varying with various organisms, may receive some explanation not only by the set of the lines of least resistance in the several anatomical systems of which the higher organisms consist, but also by a study of certain other facts in biology lying as deep as diseases or anatomical systems.

Biologists[1] tell us that there may often or generally be "discontinuity" between the arrangements, or related compounds, mechanically stable under various conditions. Either of two arrangements may be relatively stable, but nothing between them; so that the transition between them can only take place by a swift passage. If this be a true view of biological variations it may have truth likewise in respect of disease. The most stable attitude of the bodily functions is no doubt the position we call "health"; but there are, we may suppose, several other positions in which component functions have degrees of stability, and these may be the sundry kinds of disease. It may well be, again, that interferences reinforce or neutralise each other along certain lines, so that, wheresoever the disturbance, the set of functional balance, after a brief oscillation, would tend to resolve itself in a particular direction; thence, after a time of moderate steadiness it may recover the more perfect balance of health or fall into dissolution.

These opinions seem likely to illuminate some nosological riddles. We have heard a little too much of the proverb, *Natura nihil facit per saltum*, and have been led to forget that, however gradual transitions may be, intermediate phases between positions of relative stability may be so rapid as to be elusive; or again, that retrocession may take place to a certain point, whence a new position is reached.

In this light such a saw as "We are, all of us, more or less insane" takes on a new untruth, and we see how it comes that, in respect of mental and other disease, there is not in practice the difficulty which laymen assume of definitely recognising perversions from the normal. Theoretically, of course, "borderland phases" must occur, but they may not be persistent or frequent enough to embarrass us, and a new position of relative equilibrium may be reached so quickly that intermediate positions, like the flap of the wing of the albatross, are unperceived. Even thought runs, no doubt, in certain grooves. It is not to be supposed that our senses have continual cognisance of every property of things, or exhaust every possible combination of them. We are, as artists, consciously or unconsciously, ever selecting. Moreover, in our development our thoughts have probably followed certain lines of balance, cohesion, cleavage, or what not, consisting either in the physical basis of life or in the conditions of the medium. Thus every old fancy may be said to have some quality of science in it. But whether the

[1] Mr. Galton and Mr. Bateson (*Materials for the Study of Variation*, Macmillan & Co., London, 1894) have dealt with this subject before me, but with other aspects of it.

inclination to particular attitudes be inherent in the structure of living molecules, or arise in the same way as the differentiation of the several anatomical systems, or be impressed upon the organism by the prevalences of certain combinations of parts in the medium, or be again but an aspect of inertia, is not important to my argument, nor are these, indeed, soluble questions at present.

These considerations indicate the factors which make classification and diagnosis possible; perturbations tend to fall into groups which can be arranged in classes by likenesses and separated by unlikenesses. In the earlier stages of pathological knowledge, stages we have scarcely left behind, classification of symptom groups could only be made by reference to superficial and obvious features; for instance, scarlatina was confounded with measles, typhus fever with typhoid; all eruptions on the skin were classed together, — small-pox and impetigo, psoriasis and leprosy, and so forth. Even yet we put together certain syphilides and certain tubercular eruptions, and these again with other skin affections, and so on; and convenience, as I have said, may often continue for a while an arrangement which began in ignorance.

As our insight, however, becomes more penetrating, we detect resemblances more and more profound, and very commonly profound resemblances between diseases so unlike on the surface that we may hesitate at first which signs to follow. In the biological sciences, however, classification consists in the discovery of the profounder resemblances which have a wider bearing and indicate the remoter genetic origins. Clinical diagnosis, however, is not investigation — a distinction some practitioners forget; diagnosis depends not upon all facts, but upon crucial facts. Indeed we may go farther and say that accumulation of facts is not science; science is our conception of the facts: the act of judgment, perhaps of imagination, by which we connect the unknown with the known.[1] As pathology advances we detect still deeper affinities, still more permanent qualities in disease, and we form more natural classifications — classifications, that is, which depend less and less upon those superficial characters which are more likely to be products of accidents; diagnosis is the art of placing any given morbid group in the class to which at bottom it is most akin.

An explanatory classification of disease must rest, then, upon such an analysis of all life, whether animal or vegetable, as may enable us to trace the more intimate processes of disease, beginning with those of widest generality and moving onwards to the more complex. Fever, for example, is a symptom group of wide generality, and may be found in its degree no doubt in all warm-blooded animals, possibly in all animals which possess a nervous system; biologists have, indeed, inquired whether even in plants, or parts of plants, oscillations of

[1] "We cannot describe a fact without implying more than the fact" (J. S. Mill, *S. of L.*, vol. ii. p. 189, ed. 1872). Whewell repeatedly enforced the same truth, saying that comparison precedes induction, and that every record of an observation implies a comparison (*Phil. Ind. Sci.*).

temperature inco-ordinate with that of the surrounding medium may be detected during rapid changes of the tissues. A local disengagement of heat is a factor of inflammation rather than of fever, which latter term is more properly applied to the irregular propagation of heat waves in a system integrated by blood-vessels and nerves. There is a point where differentiation of fever from inflammation has not begun — where destructive changes for lack of integrating machinery cannot maintain their balance by diffusing their vibrations; when component parts fight as individual members or clans, and not yet as a national regiment. Inflammation, then, is even a more general term than fever.

Proceeding farther we find that fever forms part of a large group of maladies within which sub-groups are made according to more and more special differences. Broussais, deplorable as was his teaching on its therapeutical side, destroyed the idea of Fevers as several morbid entities: an immense service to nosology. We now know that cow-pox and small-pox, widely different as they superficially appear, must be classed together, because the processes in the cow and in men follow like initial causes; although, owing to differences in the media, they reach the surface in widely different forms. Within the memory of living physicians Mr. Hutchinson and others have impressed upon us that syphilis, widely eccentric in its superficial aspects, profoundly resembles such febrile diseases as scarlet fever and its kin, and is to be classified with these. The various phases of tuberculosis have still more recently been fitted into a serial order [*vide* art. "Tuberculosis"], and the malady as a whole carried into the same class of syphilis, small-pox, scarlet fever, leprosy, and so forth, — a class presenting the widest differences in the superficial features of its members. Tuberculosis and syphilis are now indeed recognised as the most exemplary instances of a nosological "series" of which we have cognisance.

When we turn to consider the forms in which diseases present themselves to the eye, we shall find that, even within the limits of the most definite kinds such as small-pox, no two cases are identical; and in kinds of more aberrant habit, such as syphilis, the unlikeness of cases is so marked that many of the various phases of this protean malady have been fitted into the series within the last few years. We must not suppose, indeed, that our observation of this series is even yet complete. For not only may corresponding members of two or more series of morbid phases differ in degree, but one or more members of the series may be absent — scarlatina may occur without rash, whooping-cough without whoop, angina pectoris without pain, migraine without headache, and so forth. Only by a study of genetic affinities can we dispose such cases in proper serial order; and some symptom groups, no doubt, are yet undistinguished, or if distinguished, are not yet placed in a series. The obscure series which we call gout may yet receive many more affections within its limits — attributions perhaps as unexpected as was that of "pathologists' warts," when this deformity appeared in the series we call tuberculosis. Many skin diseases have yet to find their places in series of

affinity, places which will be found for them when their causation, immediate and remote, is better comprehended. A description cannot, of course, be complete until our knowledge of morbid processes is complete, indeed, classification by genesis, being the expression of the order of our thoughts, is but the form of such knowledge, and it is by the study of aberrant processes that we may often detect the more intimate kinships. When morbid affections are all plotted out in serial order the number of such series may turn out not to be large, and the fashions of disease may indicate the several lines of cleavage or paths of least resistance in each organism or class of organisms.

If I may convert Whewell's fine figure to my present purpose, I will compare the field of disease to a large woodland country in which woods are seen of various sizes and kinds occupying hills or valleys in several masses; in places the confines are definite, in other directions smaller tufts of trees and scattered trees so diversify the intermediate tracts that we cannot precisely say where one wood ends and another begins. So again in respect of the kind of trees: on the limestone uplands we may see beech, fir on sandy knolls, elm and oak in the loam or clay of the lowlands, yet even of these kinds it may be hard to mark the limits, so gradually may clay pass into sand, or sandy clay blend with the lime into marl. So likewise with the various distribution of the waters we find other changes in the character of the vegetation, whether of the trees, of the shrubs, or of the herbs, which again confound the superficial observer by apparent caprice. Yet to one who has penetrated to the underlying facts of causation that which seemed confusion falls into order.

Once more; as these underlying and antecedent conditions of land and water do not fall apart or together by haphazard, but are likewise obedient in their turn to yet profounder series of antecedent changes, so oak, elm, beech, pine, and the rest are not flung together pell-mell, but grow in divers groups, which are repeated again and again wherever the underlying conditions repeat themselves, though never perhaps with identical repetitions: so the groups of symptoms which we call disease, if never identically repeated, because their antecedents may never be identically repeated, yet tend, as I have said, to manifest themselves in sets or in recurrent series of approximate resemblance. Now the forester, if ignorant of causation, yet learns to note the recurrence of these patterns, and the discovery is valuable to him for many practical reasons. By his practised eye the various contents of a group of trees would be thus recognised at once from previous experience, and he would be disposed to set up types in his mind, types of the natural associations of trees and plants with which he is already familiar. He might give names to these recurrent groups, as we name our symptom groups, and would speak approvingly or disapprovingly of individual groups as his convenience was favoured by the sum and qualities of the several kinds of trees which enter into them. Aberrant and defective groups would offend his practical mind, and he would gladly have all conform-

able to his main patterns, that descriptions and recognitions might for practical purposes be more easy.

Thus nosologists have been disposed to set up "**Types,**" and to look for the repetition of these types for purposes of recognition and practical uses.

If by the word "type" we mean no more than a prevalent and recurrent group, a common order of symptoms, we may thus refer diseases to types. But we run into two dangers by so doing: we tend to undervalue diversities and the teachings of diversity, fixing our eyes on the nuggets and forgetting to test the "tailings"; moreover we keep up the error connoted in the word "type," which comes down to us from the Platonist schools of philosophy. Diseases are not cast in a mould; nor would any one now affirm that behind phenomenal groups there exists a transcendental type towards which any particular embodiment is an approximation; although biologists of the school of Owen used language very like it not long ago, and the language of some of us, even if we do not talk of the "archi-" or "schematic mollusc," implies the same thing still. We use the words "type" and "typical" too often, and bring with them something more than the notion of a *mean*—some sense of approximation to or falling away from a standard or conceptual model. Teachers who would deny that they apply the term "scarlet fever" to a type in the sense of an ideal standard, yet themselves use and allow their disciples to use the word "type" in such a sense. On every page of a student's note-book we see the phrases "a typical case" or a "non-typical"; by the former some students seem to indicate a complete case, one, that is, which presents every symptom ever seen in the disease, others a case presenting a mean of them, and better called an ordinary case; others such a case as their teacher or their book sets forth; and lurking in the minds of most of them is the notion that there are real standards, or architypes, to which disease ought to conform, a notion which tends to blind them to the continuity of nature and the modes of causation. Description by "type" lends itself, then, rather to the epic of disease as presented in those "systematic" lectures on medicine which are mischievous to beginners, and except in the hands of teachers of fresh and original gifts, do on the whole more harm than good, preferring academic reasoning and pictorial description to the place of immediate observation and measurement at the bedside or in the laboratory.[1]

Of the confusion which this term brings into our thought the discussion on "change of type in disease" is an example. Physicians try to conceive some standard to which a disease approximates, so that a change of type means generally a change of the features of this figment in the mind of the speaker. Thus there are as many types of disease as there are varieties of individual imagination. A change of type in a scientific sense is a "pseud-idea"—one which eludes analysis and definition. If we thoroughly realise that diseases are but so many attitudes

[1] *Vide* excellent remarks on systematic lectures on medicine by Sir J. Russell Reynolds in his Address to the British Medical Association in London in 1895.

of men we realise the correlative of this that there can no more be a standard pattern of disease than a standard pattern of man. That the functions even of a peculiar sort of man — Englishmen or Frenchmen, let us say — preserve a constant centre of gravity is highly improbable, as improbable as that circumstances should be permanently uniform, or that differential evolution should bring about no changes in the relative values of component organs *inter se*.[1] Man, even the most secluded and protected of mankind, has advanced or retrograded, and at various rates of acceleration; it has never been alleged, even of an Andaman islander, that he has stood still. I conceive that in the minds of the able and accomplished physicians who somewhat polemically declare that "disease has not changed its type" there survives still — if unconsciously to themselves — a belief that disease is an entity which so dominates mankind and its circumstances as to impress a large measure of uniformity upon the phenomena of their interaction. Otherwise it seems to me they would hesitate to assert that every perturbation preserves a constant mean rate, and every deflected molecule a constant mean distance from a centre of gravity which never shifts.

Yet, if we teach ourselves to regard diseases as oscillations of actual men and women, to assume a constancy of these attitudes is to assume a constancy of the kinds and generations of men, and a constancy of the circumstances under which they live. If the whole argument be not a dispute with windmills, at any rate it will not do in the same breath to denounce the mischief of "modern civilisation."

What ought physicians to mean, then, when they speak of types; and what shall we lack if this term be denied to us?

Now, in any disease, the more closely a particular symptom is concerned with the functions of the organ affected, the more frequent will be its occurrence. In other words, if a large number of cases in which a certain organ is affected were arranged in order of the intensity with which the direct functions of the organism are affected, it would be found that in the more intense cases certain symptoms were universal or very frequent, and that as the intensity of the infection fell off, so also did the frequency of the occurrence of the symptom noted.

The organisms of individuals are variable in themselves, and are subject to disturbances which are not identical in each instance; but a large number of observed cases of any disease may be grouped about a certain "morbid mean," and any particular case of disease will naturally be compared with the "morbid mean." Any symptom may vary in excess of or defect from this morbid mean, and thus the morbid mean forms a convenient standard for expressing to our minds the set or bent of the phenomena.

By a typical case, then, we ought to signify (for we use the word very inconsistently) a case in which the symptoms do not differ largely from those occurring in the "morbid mean." As parallel instances, we

[1] *Vide* art. on "Typhus," in which Dr. Moore tells us that this symptom group varies with intellectual cultivation. This is certainly my experience also.

may take the variation of the stature of the men of a nation about a mean, or the distribution of bullet marks on a target.

Not only this question but many others also might be explained if by plotting out measurable symptoms in curves we could get the mean intensity of each and the amount of its variability; and could determine whether the measures are symmetrically arranged about this mean. To form such a curve the measurements would be set out along the abscissa, and the numbers of instances as ordinates. This is, however, too difficult an undertaking to discuss here, even were I capable of its discussion.[1] We have also to bear in mind that the treatment of statistics is somewhat dangerous, unless carried out by one who has some acquaintance with the theory of errors; the curves might be constructed accurately, but they might be made and used on wrong principles.

Again, a like traditional habit of thought may be seen in respect of **causation** itself. Students are taught on the highest authority to divide causes into the categories of "pre-disposing" "and exciting" — the "*causæ prevenientes*" and the "*causæ efficientes*" of the schoolmen. This habit is mischievous in two ways: to divide causes into stronger and weaker kinds keeps up that obstinate habit of men to seek in the word "cause" something more than an indication of invariable antecedence, something of a community of nature between cause and effect; and to associate with the word "cause" some notion of a casting act, of effort, or genesis: moreover, being a confusion of thought it breeds confusion. Need I say that by the causation of a thing we mean those events of the infinite past which preceded it — events which have no degree of rank or affinity, either within themselves or in respect of the thing under observation, and whose invariable precedence is a mere matter of routine experience, and not of generation, enforcement, or even of colligation. Some of the antecedent events are nearer, others are more remote; some vast sections of the system we take for granted, others which immediately concern us we quote; but there is no difference of quality — indeed, the same event may be called a "predisposing cause" at one moment and an "exciting cause" at another: a certain coccus on one day harmlessly traverses the lung, on the next a chill and the coccus together precede a pneumonia; which of the two is the exciting cause? Whichsoever comes first, some one may say; but what if they arrive at the same moment? The distinction is of course absurd. We sometimes even hear of a "plurality of causes," or that one of two or three "causes" might have produced a particular result. This is loose thinking; a certain general result — such as fever — might have been caused in this way or in that, but a "case," with all its individual characters, could have had but one set of antecedent phenomena and no other. Why this is we know not; that so it is, experience hitherto has taught us; and upon this experience we make our forecasts.

[1] I may refer the inquiring reader to a paper by Prof. Karl Pearson in the *Proc. Royal Soc.*, January 24, 1895, entitled "Mathematical Contributions to the Theory of Evolution;" although this paper is not written with a view to medical applications, yet the principles set forth in it underlie all applications of the method.

Another otiose distinction is made in the formal separation of signs and symptoms — signs being matters rather of direct, symptoms of inferential notation. The adjective "physical" makes matters worse, and yet I have heard many a student worried by such distinctions, and have even seen questions on the distinctions in an examination paper! A cough or a pale cheek is of course as much a "physical sign" as a mitral murmur; everything that befalls a patient is a "symptom," and his symptoms are the signs of his malady. Strictly speaking, health is a symptom group as well as disease, and this we must remember although common usage restricts the word to morbid incidents.

From what has gone before it becomes evident that all efforts to **define diseases** fully are in vain. The love of definition comes from the Socratic School,[1] and definition is absolutely necessary to settle a use of words, or of certain abstract conceptions, such as line, point, molecule, and the like, which are used as counters in reasoning; these words and conceptions are arbitrarily adopted, and their use must be made precise by the logician. But to define a disease is to build the wall round the cuckoo: natural processes will not be thus impounded; they are infinite and elusive. To define is to pretend to sum up knowledge, or at any rate to enumerate likenesses and unlikenesses which are inexhaustible; we are no more in a position to define diseases than to define dogs and cats. The use of "definitions," like the use of "types," leads the student to form conceptions which interfere with his appreciation of the infinite variety and gradation of natural processes; like the use of "types," it leads to contemplation of *Krankheitsbegriffen* rather than of *Krankheitszustände* — of *entia* rather than of *fientia*. The aspects of disease are not to be likened to a picture gallery in which every set of impressions is contained within its own frame. The "definitions" of systematic writers on disease are of course no more than brief descriptions, and as such are no doubt useful as mere indications of subject matter.

To sum up: disease is a state of a living organism, a balance of function more unstable than that which we call health; its causes may be imported, or the system may "rock" from some implicit defect, but the disease itself is a perturbation which contains no elements essentially different from those of health, but elements presented in a different and less useful order. Diseases, therefore, have no analogy with the genera and species of the biologist. They may be arranged for convenience of reference by any external character, such, for example, as locality; but a natural classification of diseases is an arrangement of them in order of genetic affinity, and is a description of their causation. Diagnosis is the recognition of a disease already classified and the reference of it to its place, and thus differs from research or discovery. Classification is a measure of our knowledge of the pathology of all organisms, and a pathology limited to man, like a geocentric astronomy, is, or ought to be, a notion of the past.

[1] δύο δ' ἂν ἀπόδοιέν τις Σωκράτει δικαίως· τοὺς δ' ἐπακτικοὺς λόγου, καὶ τὸ ὁρίζεσθαι καθόλου. — Arist. *Met.* xii.

The causes of diseases cannot be divided into categories; causes are merely the antecedent phenomena — the routine found by experience to be invariable. Although symptom groups tend to run in sets, yet it is with much inconstancy, infinite variety, and manifold transition; so that although a disease may be summarily indicated by some prominent features, yet to define it is a bootless quest; a definition cannot be regarded as a schedule.

Are then symptom groups so fluid that we can have no **nomenclature?** In so far as organisms are differentiated into systems, and their functions into departments, their perturbations will have some corresponding orders, and appear in groups which more or less repeat each other; in other words, the more complex the organism the more differentiated its symptom groups. For instance, a blow upon the head of a man is followed by a group of changes different from that which follows a blow upon his spine or abdomen; indeed, if the violence of the blow be given, the main characters of the resulting group in each case may be foretold with some approach to accuracy. As we descend from man to lower animals, these results will have a more general character and their groups be less definite.

Again, symptom groups can be arranged in an order beginning with the most general and ending with the most special. Fever, for example, is a group of wide generality, and is found at any rate in all warm blooded animals; probably heat-regulation or tissue stability is inherent in and conditioned by the very existence of a nervous system. The extraordinary manifestation of electric control in certain fishes also indicates to us that even cold blooded vertebrates have in electric regulation an analogous faculty. So far as I am aware, however, no experiments have been made upon local and general fluctuations of temperature in cold blooded animals subjected to catabolising agents, though tissue changes which occur under such influences are described by Professor Adami in his article on Inflammation in this volume. If fever be a member of the class of most general symptom groups, the elaborate automatic actions of certain human epileptics might be taken as instances of highly special groups of disordered functions, and between these extremes we may distinguish multitudes of groups of various stages of complexity, not by any means, as I have said, sharply defined one from the other, insensibly rather melting at their limits one into another, yet having uniformity enough on the whole to admit of naming in sets. "Well-marked cases" are probably those in which a like perturbation is felt especially by one organ, or by one set of organs; a uniform irritant falling precisely upon the same spot in the body must produce a group of events only not invariable in so far as the organism may be inconstant. Differences of conditions, however, which to our eyes are apparently very small, or even elusive, may and often do impress so great a change upon the features of definite perturbations in definite spots as to blind us to the underlying similarity of causation.

Not only, for example, may a morbific agent set up in one kind of mammalian animal a group of symptoms bearing little superficial resemblance to the group set up by the same agent in another kind; but, as the instance of the tsetze fly, among many others, shows us, the resulting syndroma may have widely different characters in the several varieties even of the same species — nay, in individuals of the same variety reared under different conditions. The so-called protective inoculations may be cases of the same order, though the relations of artificial to natural immunity are not yet made clear; the former seems hitherto to be of a more temporary kind than the latter.

Symptom groups, then, differ no doubt with the intimate form of grosser or finer parts in the various organisms, and every symptom indicates molecular disarray somewhere, could we but detect it; chemical and microscopical discovery, therefore, as they reveal more of such differences, will explain more of the variations of disease — for illustration's sake I may refer to the investigations of Metschnikoff, Kanthack, Hardy, and others on the blood corpuscles — yet we have seen already that variations in morbid phenomena bear no direct relation to the lines of obvious anatomical structure, and may vary enormously with peculiarities of organisation, chemical or other, which are so latent as hitherto to have escaped our analysis. If, indeed, we may properly appeal to protective inoculations in this place, the modified qualities of the contrasted animals, however recondite, may not be very profound or permanent.

When speaking of classification, I indicated these difficulties and the labour of detecting underlying similarities between groups of phenomena apparently disparate, and I will not enlarge again upon the same difficulties in respect of naming. We cannot name a series until we have laid down the main lines of it, and as meanwhile we must make provisional classes, so we must make provisional names. Descriptive names cannot be given until we have relatively complete pathological explanations; but by pathological explanations I mean no more than the formulation of series; or, in other words, the discovery of the causation — of the "antecedent routine," as Prof. Karl Pearson would say.[1]

Those nosologists are not unreasonable who now cry out for names which shall indicate pathological characters, but they anticipate our powers. Until we have set forth the routine of events such names are impossible, or only possible partially and in so far as we have made out some fragments of the "routine." To compare ethnology with pathology, let us suppose that an ethnologist of the linguistic school had fifty years ago discovered the Basques and called them Mongolian. Later ethnologists, putting language in a much lower place as a test of race, would supplant this name by another — say by the present name, "Basque." No sooner is the former name uprooted, and the new name affixed, than comes the craniologist to tell us that this people is of mixed race, and that distinctive names for at least two stems are

[1] *Grammar of Science.* London, 1892.

required, and so forth. Now, names are not easy to attach, and when attached are still harder to get rid of; moreover, in the supposed instance, the name "Mongolian" would, during its existence, not only be defective as an index of quality, but positively mischievous as teaching some positive error — the name "Basque," on the other hand, which conveys no ethnological meaning, being in this respect a better one.

Thus it is in the nomenclature of disease; to give pathological names prematurely may be to teach error immediately and persistently. By the illustrations I have used above, I have indicated that pathology has yet formulated but few series or even large segments of series of ordinary morbid phenomena. Events and startling features of the greatest import to us and to our patients come before us daily, and many times a day, and cannot be linked on to any other groups with which we are familiar.

Before permitting ourselves, then, to fix names significant of current hypotheses upon symptom groups not even half understood, may it not be well, until our knowledge is enlarged, to wait and be content with some name that is but a label? Nay, it is undesirable even in our merely provisional and descriptive names to connote too much; in so doing we may combine parts of different series the concurrence of which is accidental. Take, for example, the disease often called exophthalmic goitre; this name, given descriptively, is bad because as a descriptive name it postulates two events, either of which may be absent from the group, while it omits the cardiac events which are at least of equal importance. Had a pathological name been given matters would have been worse still, seeing that at least three mutually exclusive hypotheses are on foot. Is it not really more scientific after all to be satisfied for a time with such a name as "Graves' disease," which sufficiently indicates the inconstant group of events we have in view, and commits us neither to a fixed order in the group nor to any premature classification? Every physician, again, in his tractable moments will admit the usefulness of such a name as "Bright's disease" which, until the pathology of kidney disease is better understood, saves us from tossing on the conflicting currents of interstitial, of glomerular, or of tubular nephritis. Dr. Dickinson, in an article in this work, has deliberately preferred the name Lardaceous Disease as one which in the present state of our knowledge commits us to no "notiones temere à rebus abstractæ."

But, it is argued, these names may confer an immortality on the wrong man! Well, oblivion blindly scattereth her poppies: yet after all, is this often so? These names may occasionally violate the strict order of priority in discovery, as do the names of capes and islands; but the man who attaches his name to a discovery usually deserves it. If the New World had been called after Columbus, neither Sebastian Cabot nor Amerigo Vespucci would have had reason to complain. Neptune had often been observed before it was "discovered"; and a recent writer happily said concerning Fraunhofer's lines, "Wollaston

saw them, but did not discover them." There were Brights before Bright, no doubt; but the great Guy's physician worked out that which previous observers had not genius or energy enough to reveal to mankind.

And, after all, these names are, as I have said, but provisional tickets, and by no means always dedicatory — as measles, shingles, epilepsy, and the like. Such a label as "Graves' disease," when it has served its temporary purpose, will give way to a pathological name when the series is discovered in which this malady has its place, and its position in that series is plotted out. Are nosologists so ignorant, then, that as yet we can have no scientific nomenclature? Can none of our names be an intellectual instrument? By no means; but we must be content to give such instrumental names to the simpler diseases, and thence cautiously to the more complex, remembering that to name scientifically a disease of complex causation is to suppose that pathology has advanced far beyond its present stage.

Meanwhile, beside the ticket names, we have some, such as chorea, which, although given in ignorance of the nature of the malady, are fairly well descriptive; paralysis agitans is another good name of the kind; anatomical names also, such as bulbar palsy, disseminated sclerosis, and the like, are largely displacing those descriptive of symptoms — displacing, I say, and not superseding, because symptoms will probably hereafter be grouped under general and special heads from a clinical point of view, such as modified movements, modified sensations, modified reflexes, modified secretions, and so forth. But with all this we should fall short of any indication of general pathological characters — for instance, mischief in one anatomical seat, say in a joint, may be primarily of traumatic, chemical or microbic causation, and yet at certain stages produce similar modifications of motion and sensation. Identical or closely similar results may be reached from distant, and even widely different starting-points; and we come back to the conclusion that in respect of most diseases we are ignorant of the series to which they belong. We can give a clinically descriptive name to "general paralysis"; or we can pathologically call it "chronic encephalitis," but we have not learned to what series — syphilitic or other — it belongs; and until we know this we cannot finally name it.

A name is not complete, therefore, unless it indicate the tissue elements primarily engaged, and the series of which the affection forms a part. But the subject is far too extensive and various, and our knowledge too small to make it profitable to pursue the matter further in this place; indeed it cannot be fully discussed without a survey of that field of comparative nosology — of the symptoms and the causes of them in all organised beings — the exploration of which is scarcely yet begun, unless it be in respect of certain diseases of animals and plants which interfere with our industries. Pathology itself remains in much the same merely "anthropocentric" and descriptive stage as was anatomy fifty years ago; but its morphological stage is already initiated.

Of our **Terminology** I have little to say — technical terms are more fluid than names, and are undergoing continual modification as our knowledge increases. As Dr. Kanthack incidentally discusses some weak points in our terminology in his article on the General Pathology of Infection, I will not speak so fully as I had intended on this subject. The improvement of our terminology is much impeded by the loose clinical slang which too many teachers allow their pupils not only to use at the bedside, but to enter in their case-books also. Colloquial vulgarisms, effete terms of logic, relics of humoralism and pseudo-scientific phrases, make up a large part of the language of the wards, and so long as our teachers countenance, and even themselves use such slovenly language, so long will students be content with it. It is but fair to add that Medicine is not a subject in which terminology and nomenclature find their best exemplification: the matters of our inquiry, not having relatively fixed specific characters, do not lend themselves as yet to the construction of an appropriate terminology. If, for instance, we seek to affix a constant termination, such as "itis," to signify all kinds of inflammation, we are met by the inconstancy of the meaning of the term "inflammation," and by its possible confusion with the encroachments of competing tissues and with acute degenerations. We cannot yet say when fibrosis is "inflammatory" in origin, or when, on the other hand, it may be relatively atrophic, for we are also uncertain in our use of the terms atrophy or hypertrophy. Still there is no reason why in the near future these terms should not be better defined. I am not without hope that the work of Professor Adami and Dr. Mott in this volume may go far to help us on our way.

To illustrate at length the looseness of our terms, and the errors which arise from the equivocal use of any of them, were an undertaking far beyond the space at my disposal. The student finds his notorious security in terms,[1] because he has not learned that one term does not always carry one and the same meaning. As Mr. Grote has said, no part of the Platonic writings is more useful than those Dialogues in which the disputant is forced to feel how imperfectly he understands the phrases in common use. But it was reserved for Aristotle to recognise "equivocal terms" as a class, and to assign to them a particular name. Until we are at one in our use of terms we cannot formulate propositions as true or false; we cannot, that is, combine our terms as subject and predicate. As was said of another matter, medical discourse and medical literature are "pervaded by assumptions": I would therefore earnestly appeal to all bedside teachers to compel their pupils to look every term well over as it comes to them; to scrutinise it obversely, reversely and edgewise before using it as currency. As things are, candidates for degrees use arguments based upon equivocal terms, shelter themselves under phrases which save them the trouble of

[1] Need I quote from Faust the well-known lines? —

"Denn eben wo Begriffe fehlen
Da stellt ein Wort zu rechten Zeit sich ein."

thought; and are disposed to feel as injured as Thrasymachus if these current phrases are challenged.

I have spoken of the causation of disease; I have shown that diagnosis is the practical aspect of classification; I will now conclude with a few words on **Prognosis.**

A living being is found in a given abnormal state (diagnosis); we have then to find how this came about (ætiology); and, thirdly, we have to foretell the state in which the creature will be at a given future time. Such forecasts are already possible when we deal with large numbers. If we wish to know the mean duration of life in a young man of twenty years of age we have tables at hand which will inform us; if any particular young man be associated with a sufficiently large number of others like himself, we can deal with him on a definite "curve of frequency."

But when a particular patient comes to a physician he is not satisfied to know the mean expectation of a thousand sufferers in his case, but he will insist upon knowing the future part of the curve of his own individual phases. If he present himself before a physician of large experience he will get some such estimate — an estimate fallible, it is true, but in many cases having sufficient probability to justify the patient in laying out his plans for the future with some confidence.

Now, how is this attained? Let us go a step farther, and consider a sub-class of the young men aged twenty, namely, young Englishmen; we may still find statistics for this purpose, and give an estimate of the mean duration of life in this sub-class. Suppose that we go a step farther still, and construct a class still more subordinate, namely, of young medical students, or of young medical students in a certain university, or of young medical students classed as students, oarsmen, or cricketers, and we may still find something like statistics to guide us. But in thus subdividing our classes, we shall soon arrive at sub-classes for which registered statistics are no longer available — the numbers are too few, the cases too special, or they have not been tabulated. Thus we approach the prognosis of individual cases, and rely more and more upon the quality of the observer. In discussing this matter with Dr. Venn, it appeared to us, nevertheless, that the method is still one of statistics — one of conscious or unconscious abstraction, based upon numerical summary. The accumulated experience, although not formulated, is nevertheless an accumulation of records of cases — cases recorded imperfectly, it may be, but written upon the memory of a skilled observer, and of these the observer more or less automatically strikes a mean when called upon to estimate the expectation of a given life, or of particular events in the life. The observer may rely more upon his note-books, and make a calculation dependent upon their fulness and accuracy; or he may rely rather upon an acquired instinct bred of accumulated impressions upon his senses, and dependent upon the tenacity of his memory and the quickness of his observing faculties: still in either case — whether the judgment be more automatic or less

automatic — it is based, in the last analysis, upon statistics, and the result has the more validity as the number of observed cases increases.

Again, this acquired judgment does not wholly die with the individual.[1] The instructed observer formulates certain middle axioms which he illustrates at the bedside before his pupils: using these with discrimination, his pupils revise, confirm or modify them; and thus something like a body of quasi-statistical knowledge is handed down from generation to generation. As observation becomes more accurate, as the number of observed cases increases, and as classes are better and better distinguished, the nearer will the physician be able to approach an accurate prognosis — though the time when any sufficient rule can be applied to individual cases must long be out of our sight; and the application of any approximate rules must long be subordinate to the instinctive tact of the educated physician himself, who alone can apprehend the sum of the peculiarities which must modify their application to individual instances. Like the so-called cumulative photographic image which results from the blending of many superposed faces of the same kind, there grow up before the mind's eye of the educated physician, images of this morbid facies, and of that, to which he refers individual instances; and he pronounces his opinion of the state and probable future phases of individuals as these severally vary this way or that from the standards within himself.

T. CLIFFORD ALLBUTT.

[1] Dr. Venn writes to me on this passage as follows: — "I think this is very important. I have often been struck by the way in which an apparently subjective judgment can be perpetuated, as an almost objective standard, within some specially trained class of persons, who are in frequent communication.

In order to avoid frequent interruption of the text, the Editor has only inserted the numbers indicative of items in the lists of "References" in cases of emphasis, where two or more references to one author are in the list, where an author is quoted from a work published under another name, or where an authoritative statement is made without mention of the author's name. In ordinary cases an author's name is a sufficient indication of the corresponding item in the list.

DIVISION I

PROLEGOMENA

MEDICAL STATISTICS

In this paper the term "Medical Statistics" includes statistics of diseases in their relations to etiology, symptomatology and results, as derived from comparisons of records of cases of such diseases. It will also be necessary to consider some of the results of mortality statistics, derived from a comparison of the number of deaths in a given time with the number of people among whom such deaths occurred; and of morbidity statistics, derived in like manner from comparisons of the number of cases of disease occurring in a given population in a given time; in a broad sense, the term medical statistics no doubt includes both mortality and morbidity records.

The essential difference between the methods of medical statistics and those used by the vital statistician is that the former have usually no reference to population data. The medical statistician inquires how many cases of pneumonia, or of consumption, or of Bright's disease have been under observation; what proportion of these have been of certain ages, or races, or occupations; and what proportion have recovered or died under certain modes of treatment: but, as a rule, he has no data to show the number of cases of pneumonia occurring among a given number of people who are between forty-five and sixty-five years of age, he cannot therefore deal with ratios to population, which are the basis of most of the work of the vital statistician, who would inquire as to the relative probabilities that an Irish male between forty-five and sixty-five will have pneumonia as compared with a German male of the same age group; or that a plumber between twenty and forty years old will contract pulmonary phthisis as compared with a carpenter of the same age.

The physician finds from hospital records that in each 1000 cases of cancer in males a greater number occur in persons between the ages of fifty-five and sixty-five than in any other age group; while the vital statistician, from the records of deaths, finds that the mortality from cancer steadily increases with advancing years up to the age of ninety, and concludes that the reason why there are few cases of cancer in people seventy-five years of age and upward is simply because there are comparatively few people of that age. In the tabulation of the

returns of cases of acute rheumatism in the *Collective Investigation Record* it is shown that of the 655 cases recorded 71 were in domestic servants, 16 in agricultural labourers, 10 in grocers, etc., and the conclusion is drawn that domestic servants are especially liable to rheumatism, and that this may be due to their greater use of alcoholic drinks.

Such a conclusion has no basis in the figures, because we know nothing of the proportion of domestic servants attended by the physicians who made the reports, to the total number of these servants in existence, or to the number of servants who had rheumatism. The utility of medical statistics has not been so great as was hoped by Louis and others. As applied to the study of a disease it is necessary that the different observers who furnish the records shall be referring to substantially the same disorder of structure or function — that is, there must be a tolerably definite series of symptoms, such as occur in specific diseases and acute affections of particular organs. The statistical method is most applicable, and has proved most useful in surgical cases. With improved methods of diagnosis, the possible utilities of medical statistics are becoming greater; evidently little could be done with statistics of fevers before the differences between typhus, enteric and relapsing fevers were known; but, on the other hand, when we have discovered by experiment that a given result must follow a given cause, a few repetitions of such experiments give as great a degree of certainty as would several thousand. Statistics are useless to prove that chalk will be decomposed by sulphuric acid, and they are now of little value in discussing whether tuberculosis be caused by a particular form of bacillus; but they are the only means yet available for determining the varying degrees of immunity against this bacillus possessed by different races.

The causative influence of a given condition upon the results of a disease can only be calculated approximately, because we can never be sure that the sum of all other conditions which might influence the result remains the same in the different cases investigated; but much may be done to estimate the effects of the different conditions of the living body and of its environment upon disease, provided that we can obtain a sufficient amount of data to enable us to come within the limits of the law of probable error. This matter of the probable or possible error of ratios in relation to the magnitude of the figures from which they are derived should be kept in mind in the use of medical statistics. The most convenient method to estimate it is by what is known as "Poisson's formula," as follows: —

$$\frac{m}{q} \pm 2\sqrt{\frac{2mn}{q^3}} = \text{possible variation in proportion of } m \text{ to } q.$$

q = total number of events.
m = number in one group.
n = number in the other group, so that $m + n = q$.

For example, suppose that in 1000 cases of typhoid fever in whites

100 die, while in 1000 cases of the same disease in negroes 95 die, what is the probability of the conclusion that this disease is less fatal in negroes than in whites?

By the formula—For the whites, $q = 1000$, $m = 100$, $n = 900$, and the possible variation in the ratio $\frac{100}{1000}$ or 0·1 is plus or minus $2\sqrt{\frac{180{,}000}{1{,}000{,}000{,}000}} = \cdot 0268$, so that the death-rate might be from 0·1268 to 0·0732, *i.e.* from 127 to 73 per 1000. By the formula—For the negroes the possible variations in the ratio $\frac{95}{1000}$ is $2\sqrt{\frac{171{,}950}{1{,}000{,}000{,}000}} = \cdot 0262$, so that it might be either 0·1212 or 0·0687, *i.e.* from 121 to 69 per 1000.

The figures are therefore too small to answer the question definitely as to influence of race. But if of 1,000,000 cases in whites 100,000 die, and of a similar number in negroes 95,000 die, then the probable error for the whites becomes + or − ·000424—or from 100·424 to 99·576 per million die—and the probable error for the coloured becomes + or − ·000414, or from 95·414 to 94·586 per million die.

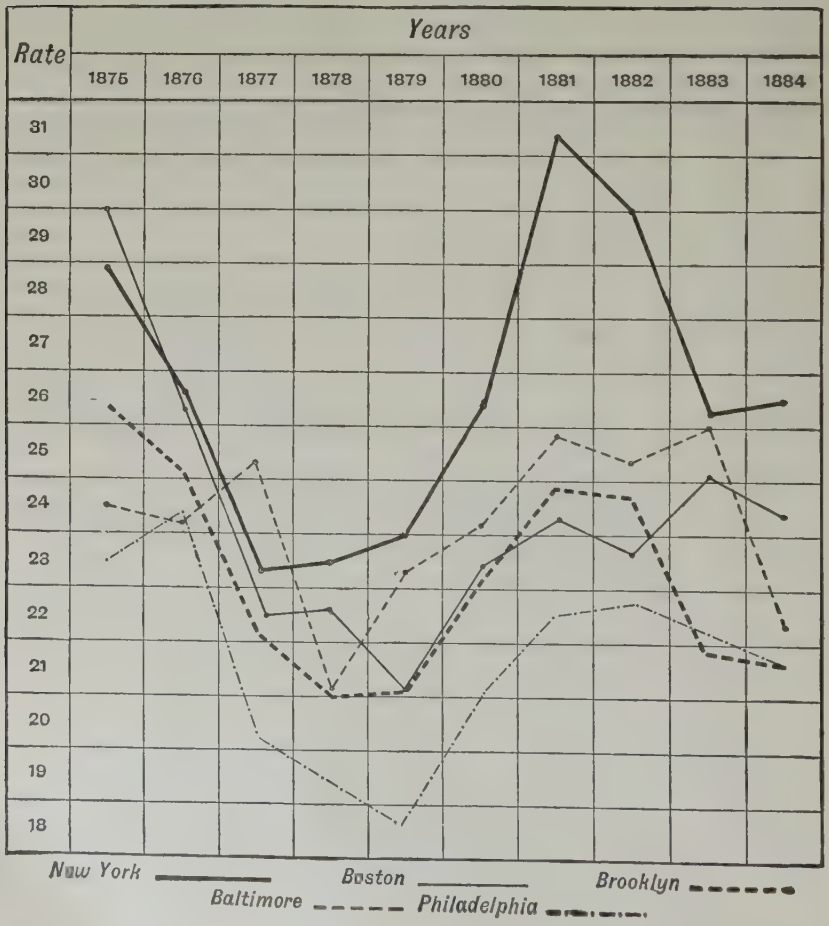
Stating these in the usual form of ratios per 1000, it would be that among the whites the death-rate is between 99·58 and 100·42, and among the coloured between 94·59 and 95·41 per 1000, indicating a definite and positive difference between the death-rates of the two races.

A special application of this law of possible error in connection with the length of time covered by the data should be borne in mind in comparing medical and vital statistics. The death-rates of a city of 10,000 inhabitants for ten successive years are much more indicative of the relative healthfulness of the place than is the death-rate of a city of 100,000 inhabitants for a single year, because the death-rate for a single year may be greatly influenced by epidemics and by meteorological peculiarities.

The following table and diagram show the relative magnitude of the death-rates in New York, Brooklyn, Boston, Philadelphia, and Baltimore in each of the sixteen years from 1875 to 1890 inclusive:—

[TABLE

Year.	New York.	Brooklyn.	Boston.	Philadelphia.	Baltimore.
1875	28·8	26·3	30·0	23·5	24·5
1876	26·6	25·1	26·3	24·4	24·2
1877	23·3	22·3	22·5	20·2	25·4
1878	23·5	21·0	22·6	19·4	21·1
1879	24·0	21·1	21·1	18·6	23·4
1880	26·4	23·3	23·5	20·9	24·2
1881	31·3	24·7	24·3	22·5	25·8
1882	30·0	24·6	23·7	22·7	25·4
1883	26·3	21·8	25·1	22·2	26·0
1884	26·5	21·6	24·3	21·6	22·4
1885	26·3	22·7	23·8	22·7	21·4
1886	27·0	22·5	22·4	20·8	21·3
1887	27·5	23·5	23·9	22·1	20·8
1888	27·7	24·0	23·7	20·3	21·7
1889	26·7	23·7	23·3	20·0	20·5
1890	26·4	24·5	23·7	20·7	23·4



It will be seen from this table that in all these cities the death-rates fell from 1875 to 1878–79, then rose until 1881–82, and then again declined. The influence which produced these great variations could not have been a local one.

What is the normal sickness rate of a people? That is to say, in a general population of 100,000, how many are constantly sick to such a degree as to require medical attendance, or to be incapacitated from pursuing their ordinary avocations? The only sources to which we can look for the answer to this question are the records of the army and navy in different countries, of certain benefit societies providing insurance against sickness, of the police force in certain cities, of employees of railroads, and of the last censuses of Ireland, of the Australian colonies, and of the United States.

The following table shows for various armies the number of admissions to treatment for sickness and injury per 1000 of mean strength in a year, the number constantly sick, the average number of sick days to each soldier, and the average duration of each case of sickness:—

Armies.	Periods.	In 1000 mean strength.		Sick Days to each Soldier of mean strength.	Average Duration of each case of Sickness.
		Admissions.	Constantly sick.		
Belgian army	1880–89	1407	28·3	10·3	7·3
Prussian army	1883–89	830	30·8	11·2	12·9
Italian army	1878–91	853	34·7	12·6	15·7
Dutch army	1884–89	906	37·0	13·5	14·1
United States (white)	1881–90	1337	43·3	15·8	11·0
Austrian army	1879–89	1185	45·3	16·5	13·4
British army at home	1881–90	820	46·0	16·7	20·4
French army	1875–84	2476	46·8	17·1	6·9
British in India	1881–90	1458	73·0	26·6	18·2
Coloured Troops.					
United States (coloured)	1881–90	1577	44·3	16·2	10·0
British troops (coloured in North India)	1881–90	1035	51·1	18·6	18·0
British troops (coloured in North Africa)	1881–90	1736	76·5	27·9	17·0

From this table it will be seen that of each 1000 soldiers serving in temperate climates about 35 are constantly sick, the figures varying from 28·3 in the Belgian army to 46·8 in the French army. It must be remembered, however, that these figures relate only to males of certain groups of ages, and of a carefully selected class of population, but of a class much more apt to claim exemption from duty on account of sickness than would be the males of corresponding ages in the general population. Taking the male members of friendly societies from the age of fifteen to eighty-five, Mr. Finlayson found that about five years of sickness occurs to each man during those seventy years; but the sickness occurring in

men from forty-two to sixty-six years of age is almost double the sickness occurring in men from fifteen to forty-one years of age. From the commencement of the sixteenth year of age to the close of the sixty-sixth the amount of sickness averages about one and a half weeks per man. (See *Insurance Cyclopædia*, vol. v. p. 83.)

In the "Hearts of Oak Benefit Society," Mr. Ralph Hardy reports (*Journal of the Institute of Actuaries*, January 1894, p. 86) that from 1884 to 1891 the total number of members was 940,224, of whom 7853 died, and 238,787 were claimants on account of sickness or disability.

The following table shows for each of certain groups of ages the number exposed to risk, the number of weeks of actual sickness or disability for which claims were made, and the number of weeks of sickness or disability per member in each group: —

Ages.	Number exposed to Risk.	Number Weeks actual Sickness.	Number Weeks Sickness per Member in each group.
19	2,007	3,241	·68
20–24	68,637	69,370	·75
25–29	178,275	164,740	·81
30–34	235,268	249,700	·92
35–39	189,502	261,428	1·06
40–44	135,164	239,682	1·28
45–49	75,441	168,242	1·65
50–54	29,567	93,373	2·20
55–59	14,054	67,679	3·13
60–64	7,712	60,926	4·74
65–69	3,418	49,278	7·34
70–74	1,001	20,448	11·50
75–79	169	3,817	16·19
80	9	181	52·00
All ages.	940,224	1,452,106	

It will be seen from this table that for those under forty years of age there was less than one week's sickness in each year, and that after this age the amount of sickness nearly doubled every ten years.

The following table gives the results observed in 311 Italian mutual benefit societies as regards the sickness occurring among 254,193 males. (*Annali di Statistica, Tavole della frequenza e durata delle Malattie, etc. Roma*, 1892): —

[Table

Ages.	Number taken sick yearly per 1000 of Number observed.	Number of cases of Sickness in a year per 1000 of Number observed.	Number of days' Sickness to each Member in a year.	Number of days' Sickness to each sick Person in a year.	Average Duration of each Sickness in days.
10–15	191	235	3·9	20·3	16·5
15–20	234	276	4·9	20·9	17·7
20–25	213	251	5·0	23·2	19·8
25–30	229	266	5·4	23·6	20·3
30–35	223	256	5·1	23·0	20·6
35–40	240	278	6·0	24·8	21·4
40–45	232	273	6·2	26·7	22·7
45–50	253	289	6·8	27·0	23·7
50–55	258	304	7·9	30·7	26·1
55–60	275	328	9·2	33·7	28·2
60–65	299	361	11·2	37·3	30·9
65–70	322	404	13·4	39·9	33·4
70–75	344	397	14·7	43·0	37·2
75–80	286	337	13·4	41·1	39·9
Ave. over 10	242	283	6·6	27·1	23·2

The following table shows the number of sick and of those suffering from accidents, per 1000 of population, in certain states and countries, as found in recent censuses: —

States and Countries.	Years.	In 1000 Population.	
		Diseases.	Accidents.
Maine	1890	12·93	·84
Connecticut	1890	15·23	·97
Massachusetts	1890	12·31	·93
New Hampshire	1890	22·09	2·41
Rhode Island	1890	18·36	1·04
Vermont	1890	28·98	1·66
Virginia	1890	16·69	2·06
Alabama	1890	15·08	1·36
District of Columbia	1890	17·08	1·56
Delaware	1890	13·18	1·45
Victoria	1890	11·36	1·97
South Australia	1890	10·98	1·46
New South Wales	1890	9·00	1·34
Tasmania	1890	8·00	1·29
New Zealand	1890	7·81	1·23
Queensland	1890	7·51	1·21
Western Australia	1890	4·85	1·03
Ireland	1891	7·12	·47

Including women and children, it is probable that for each 1000 of population under ordinary circumstances, 400 are taken sick or laid up by accidents during the year, and that about thirty are constantly sick, the average duration of illness being about four weeks.

It is usually estimated that for every case of death in a community there are two persons constantly sick — that is to say, there is an average of two years' sickness to each death; or with an annual death-rate of 18 per 1000, the average number constantly sick is about thirty-six per 1000: but this estimate is probably somewhat in excess of the true figures under ordinary circumstances, and it should be distinctly understood that it does not apply to individual diseases, but only to the whole mass of diseases and injuries. The proportion of "cases constantly sick" to "deaths" is very different for consumption, diabetes and cancer, from that which exists in diphtheria, typhoid fever and tetanus. The sickness ratios derivable from the data of those censuses in which an attempt has been made to enumerate all the sick living on the day of the census are evidently too small; but it is probable that they represent very fairly the different proportions of sickness existing in males and females of certain groups of ages. According to the census of 1880 in the United States, the proportion of sick to 1000 of population of different ages was as follows: —

Age.	Males.	Females.
15 to 25	6·9	6·8
25 to 35	8·6	9·7
35 to 45	12·2	11·5
45 to 55	16·8	14·4
55 to 65	25·5	20·4
65 and over	44·5	35·3

In the state of Massachusetts on 1st June 1890 out of a total population of 2,238,943 there were reported 41,512 sick and defective, of whom 25,490 were males and 16,022 females, giving a ratio of 23·44 for males and 23·46 for females per 1000 of population.

The ratio per 1000 at different age groups was as follows: —

Ages.	Males.	Females.
15 to 25	9·74	6·90
25 to 35	12·38	8·84
35 to 45	21·80	13·11
45 to 55	57·14	21·76
55 to 65	71·17	34·19
65 and over	96·41	60·84

In each 1000 of the total sick and defective there were as follows: —

	Male.	Female.
Total of all diseases	623·9	719·6
Rheumatism	175·8	176·2
Consumption	34·5	51·3
Cancer and tumours	9·0	36·9
Nervous system	37·8	80·7
Circulatory system	56·8	70·7
Urinary organs	48·4	22·4
Bones and joints	42·1	64·8
Total deformed, ex. spine	23·4	18·6
Total lost arms	30·6	3·8
Total lost legs	31·3	6·4
Total lame	105·6	84·0
Accidents and injuries	77·9	29·3
Paralysed	82·2	101·2

There are no figures available as to the amount of sickness among children, but it is probably much greater among them than in adult life, corresponding generally to the greater mortality of the earlier years of life.

It is not probable that anything like complete returns of sickness will be obtained in the near future for any large body of the general population. The registration of diseases will be confined to infectious and spreading diseases — that is to say, to diseases which are known or supposed to be preventable — and the more unusual the disease the more likely is the registration to be complete. In England and the United States, nearly all cases of Asiatic cholera, small-pox and yellow fever will be registered, while the registration will always be defective for such diseases as measles, scarlet fever, diphtheria and typhoid fever. The only means then at our command for calculating the number of cases of a given disease, occurring in a given community during a given time, is by taking the number of deaths reported as due to that disease, and multiplying this by the ratio of deaths to cases, a ratio obtained from hospital and other medical records, being what is called the "case mortality." This method contains many sources of error. Many forms of disease which render life more or less of a burden seldom or never appear in the registration records as a cause of death; while even of those diseases which are reported as the cause of a considerable proportion of deaths, it is usually impossible to establish any definite and certain relation between the number of cases of the disease and the number of deaths reported even for the acute specific diseases, such as scarlet fever, measles, yellow fever, etc. The mortality varies greatly in different epidemics, such variations appearing to depend partly upon particular conditions of the specific micro-organisms to which such diseases are generally attributed, and partly upon particular conditions of the people,

and the environment as to race, density of population, temperature, moisture, etc. For example, in 1867 yellow fever entered the United States by two distinct routes — one from Vera Cruz, and the other direct from Havana. At that time the United States had troops along the southern border of the country, and hence we have a series of returns showing both the number of deaths and the cases of sickness from this disease in a given population. Now in those places where the disease was of Mexican origin, the cases were more fatal than in those where it was of Cuban origin; the ratio of deaths being 400 per 1000 cases for the first of those groups, and 284 for the second.[1]

The statistics of diseases with reference to their etiology, using this term in its widest sense, have attracted much attention within the last fifty years, but the data have been derived mainly from mortality statistics. The immediate, or so-called efficient causes of disease are physical or chemical agents, micro-organisms, or sensory impressions leading to disordered brain action; but these agencies produce different effects in different persons. The same exposure to cold may give rise in one man to coryza, in another to pneumonia, in a third to rheumatism, in a fourth to diarrhœa, and in fifty others to no apparent disturbance whatever. The hæmatozöon of malaria, the bacillus of tubercle, or the *bacillus lanceolatus*, produce their specific effects in some people but not in others.

If the axiom that "like causes, under like circumstances, produce like effects," be as true for the living human body and all its parts as it is for a laboratory experiment in chemistry or physics, it follows that the different results as to production of disease brought about by the same immediate cause must be due to differences in the circumstances — that is, to differences in structure and function of the human beings upon which they act.

These differences may be inherited and innate, or connate without being inherited, or acquired after birth; and are indicated by such words as temperament, diathesis, idiosyncrasy, immunity, acclimatisation, etc. That such differences exist is well known to every physician, and he takes them into account in diagnosis, prognosis, and in hygienic and therapeutic advice. He knows, for example, that delirium in specific fevers has a very different significance in certain families from that which it has in others; that malaria and chorea affect the white more than the black or yellow races; but as yet we have little definite scientific information as to the relative effect and importance of such circumstances upon liability to, or effects of different forms of disease. Such information can only be obtained by comparing a large number of cases by statistical methods to see if any general laws can be deduced therefrom, and then studying individual cases or groups of cases which form an exception to these laws.

The influence of age upon mortality is well known, and, through the

[1] *War Department, Surgeon-General's Office, Circular No.* 1, p. xviii.

labours of W. Farr and other vital statisticians, it can now be expressed in mathematical terms, not for any single individual but for the average of a large number of people, by means of life tables. It may be summed up in the law of Gompertz, as modified by Makeham, namely, that after the age of puberty the vital power of the organism, or the sum of its powers to resist death, diminishes by a series consisting of the sum of two terms, one of which is a constant quantity, while the other increases in geometrical progression.

It is evident that the same law must apply to a considerable extent to sickness, and we have shown above that sickness rates vary with age very much as mortality rates do. The dominating influence of age upon sickness and mortality is usually not sufficiently appreciated by medical men who prepare and publish statistical records of hospitals or dispensaries. It is hardly possible to draw useful conclusions as to the mortality of most of the diseases of adult life, unless the cases and their results are given by age groupings.

The following table, compiled from the records of eighteen hospitals for the last fifteen years, indicated the differences in the fatality of certain diseases in patients of different ages: —

[TABLE

Ages.	Pneumonia.			Typhoid Fever.			Consumption.			Diphtheria.		
	Cases.	Deaths.	Rate per 100 cases.	Cases.	Deaths.	Rate per 100 cases.	Cases.	Deaths.	Rate per 100 cases.	Cases.	Deaths.	Rate per 100 cases.
0–10	2273	246	10·8	363	30	8·2	43	20	46·5	1251	725	57·9
10–20	6076	501	8·2	3787	491	12·9	4,278	1084	46·3	148	33	22·3
20–30	8726	1342	15·3	4801	818	17·0	14,504	7101	48·9	166	17	10·2
30–40	5644	1242	22·0	1170	295	25·2	11,446	6351	55·4	....	....	....
40–50	4107	1242	30·2	352	118	33·5	6,282	3627	57·7	....	....	....
50–60	2811	1134	40·3	133	54	40·6	3,386	2003	59·1	....	....	....
60–	2548	1456	57·1	32	21	65·6	1,635	1028	62·8	....	....	....

This table includes 32,185 cases of pneumonia with an average or gross death-rate of 22·25 per cent. It shows, however, that the proportion of deaths steadily increased from 8·2 per cent in the cases between ten and twenty years of age, to 57 per cent in the cases sixty years of age and upward; hence the giving of gross death-rates only for a few dozen, or even a few hundred cases of pneumonia, to show the influence of a particular mode of treatment, is almost useless. The same increase in the death-rate with increase of age is shown in typhoid fever, the gross death-rate for the 10,638 cases reported being 19 per cent of the cases, varying from 12·9 to 65·6 per cent in different age groups. In

consumption also the hospital death-rate increases with advancing age, but not to such a marked extent; while in diphtheria it rapidly falls after ten years of age. But the hospital death-rate in consumption given above is misleading, since the figures are taken from annual reports, and the same cases are reported two or three times. The hospital death-rate for 116,673 cases of consumption was 443·4 per 1000, which signifies, not that the death-rate in this disease is a little over 44 per cent of the cases, but that the average duration of the disease is a little over two years, the true death-rate being about 90 per cent.

The fatality of different diseases will, of course, be indicated in the special articles treating of them, but the following are the death-rates of a few as indicated by hospital records — age not being stated: —

Disease.	Cases.	Deaths.	Rate per 1000.
Pneumonia	36,273	9438	260·1
Typhoid fever	37,986	5657	148·9
Diphtheria	7,090	2526	356·2
Scarlet fever	5,757	737	128·0
Acute pleurisy	20,871	2229	106·7
Acute bronchitis	30,408	913	30·0
Acute nephritis	2,207	562	254·6

The following table shows the case mortality of certain diseases as shown by the Norwegian reports for the four years 1888–1891 inclusive: —

Diseases.	Cases treated.	Deaths.	Deaths in 1000 Cases treated.
Meningitis simplex (leptomeningitis cerebralis acuta)	1,311	1,015	774·2
Cancer	7,082	4,641	655·3
Croup	1,646	961	583·8
Phthisis pulmonalis	26,374	11,844	449·1
Cerebro-spinal meningitis	170	58	341·2
Puerperal fever	2,034	621	305·3
Bright's disease	7,070	1,840	260·3
Diphtheria	30,473	7,010	230·0
Pneumonia	46,085	6,873	149·1
Typhoid fever	7,467	755	101·1
Scarlet fever	24,657	1,547	62·7
Dysentery	1,013	59	58·2
Whooping cough	27,914	1,327	47·5
Pleurisy	11,659	388	33·3
Measles	36,149	1,169	32·3
Acute diarrhœa and Cholera nostras	101,491	3,212	31·6
Rheumatic fever	13,654	250	18·3
Acute catarrh and bronchitis	227,466	3,493	15·3
Influenza	93,149	794	8·5
Mumps	6,087	2	0·3

Let us now compare the number of deaths from certain diseases with the number of population in which they occurred, that is, the death-rates of the vital statistician.

The following table shows the average annual death-rates from each of certain causes per 10,000 living population, during a period of about ten years in different countries: —

Countries.	Periods.	Death-rates per 10,000 Population.												
		Aggregate.	Small-pox.	Measles.	Scarlet Fever.	Diphtheria.	Diphtheria and Croup.	Whooping Cough.	Enteric Fever.	Pneumonia.	Consumption.	Diarrhœal Diseases.	Cancer.	Childbirth.
England and Wales . .	1880–89	192	·48	4·46	3·77	1·56	2·95	4·56	2·05	10·32	17·49	7·61	5·75	1·52
Ireland . .	1880–89	181	·12	1·95	2·50	·69	2·26	3·06	1·65	5·33	20·97	3·29	3·95	1·69
Scotland . .	1880–89	192	·03	3·65	3·25	2·10	4·25	6·00	2·47	10·40	20·17	4·93	5·70	1·75
Belgium . .	1880–87	204	3·23	5·15	2·55	...	5·55	6·72	5·35	...	...	15·09	...	2·30
Sweden . .	1880–89	170	·17	1·88	5·17	5·82	7·26	1·80	2·59	...	...	4·33	...	1·17
Prussia . .	1880–89	248	·16	4·14	4·55	...	16·32	5·17	3·83	14·04	30·43	10·38	3·59	2·10
Austria . .	1877–86	307	6·13	5·04	6·15	...	16·51	11·00	7·22	...	38·76	...	4·29	...
Saxony . .	1881–89	278	...	2·61	3·84	...	15·31	2·75	2·14	...	23·84	...	7·32	...
Norway . .	1880–89	167	·06	1·06	3·67	5·54	...	1·76	1·07	7·81	13·89	...	4·99	2·07
Bavaria . .	1885–87	...	·02	3·13	2·66	...	11·43	5·00	1·70	...	27·97	...	6·46	...
Holland . .	1885–87	208	·11	3·23	2·00	...	5·00	3·36	1·40	...	19·30	22·10	6·66	...
Rhode Island	1880–89	179	·02	1·02	4·77	5·37	8·10	1·42	4·95	13·57	23·98	15·46	5·20	1·02
Connecticut.	1880–89	168	·09	·92	2·65	5·45	7·94	1·17	3·84	12·65	20·91	13·50	4·26	·98
Massachusetts	1880–89	193	·08	1·12	2·33	6·53	9·22	1·24	4·52	15·65	28·84	14·23	5·42	·91
New Jersey .	1879–88	187	·55	1·08	4·66	...	9·76	1·46	4·72	...	23·99	21·28	3·90	...

In dealing with medical statistics we usually have no data as to population, and the best rates we can obtain to show the relative prevalence of a given disease in different localities, or in the same locality at different times, are rates per 1000 deaths from known causes.

The following table shows these rates for the countries and periods given in the preceding table: —

Countries.	Periods.	Death-rates per 1000 Deaths from all causes.												
		Small-pox.	Measles.	Scarlet Fever.	Diph-theria.	Diph-theria and Croup.	Whooping Cough.	Enteric Fever.	Pneu-monia.	Con-sump-tion.	Diar-rhœal Dis-eases.	Cancer.	Child-birth.
England and Wales . .	1880–89	2·5	23·1	19·6	8·1	15·3	23·6	10·6	53·6	90·9	39·5	29·8	7·8
Ireland . .	1880–89	0·7	10·7	13·8	3·8	14·6	16·8	9·1	29·4	115·8	18·1	21·8	9·3
Scotland . .	1880–89	0·2	18·9	16·9	10·9	21·9	31·1	12·8	54·0	104·7	25·6	29·6	9·1
Belgium . .	1880–87	15·7	25·1	12·4	...	27·1	32·8	26·1	...	...	73·6	...	11·2
Sweden . .	1880–89	1·0	11·0	30·3	34·1	42·3	10·7	15·2	...	...	25·4	...	6·8
Prussia . .	1880–89	0·6	16·7	18·3	...	65·7	20·8	15·4	56·5	122·6	41·8	14·4	8·4
Austria . .	1877–86	19·9	16·4	20·0	...	53·7	35·7	23·4	...	126·0	...	13·9	...
Saxony . .	1881–90	...	9·4	13·8	...	55·0	9·9	7·7	...	85·7	...	26·3	...
Norway . .	1880–89	0·3	6·3	21·8	33·0	...	10·4	6·4	46·5	82·7	...	29·7	12·3
Rhode Island	1880–89	0·1	5·3	26·6	29·9	45·1	7·9	27·6	75·7	133·7	86·2	29·0	5·7
Connecticut .	1880–89	0·5	5·4	15·8	32·4	47·2	6·9	22·9	75·3	124·5	80·3	25·3	5·8
Massachusetts	1880–90	0·4	5·7	12·2	34·2	48·3	6·5	23·7	82·1	151·3	74·7	28·4	4·9
New Jersey .	1880–89	3·0	5·8	25·5	...	53·4	7·9	25·8	...	131·3	116·5	21·3	...

It is important to remember that a table like this does not give true mortality rates, and that the rates given by it for any given disease are affected not only by the actual prevalence of that disease, but of other causes of death, so that very erroneous conclusions may easily be drawn from them; nevertheless, they are often the only rates available, and if the gross death-rates of the different localities are about the same, or if it is possible to estimate their difference, some useful conclusion may be drawn from a table of this kind. For example, each of these tables indicates that typhoid fever caused a little more than twice as great a mortality in Massachusetts as it did in England; and that diphtheria caused about four times as great a mortality in Massachusetts as in England. Where the average annual death-rate is about twenty per 1000, the number of deaths due to a special disease per 1000 deaths from all causes should be about five times the number of deaths from that disease per 1000 of population, if the population has the usual proportions of sex and age; but this ratio is not applicable in most cases, because an epidemic of any particular disease changes the proportion of deaths from any other disease per 1000 deaths from all causes, while the number of deaths from that other disease may have remained the same per 1000 of population; and the proportion of children in a locality will greatly influence the death-rate from diphtheria and scarlet fever, just as the proportion of old people will influence the death-rates from pneumonia and cancer.

Next to age in the importance of its influence upon disease is heredity. At present almost the only data we have on this subject relate to race differences; but there are equal, and probably greater differences in families of the same race, recorded only in a vague way in the memories of old family practitioners.

Professor Allbutt has pointed out that studies of hereditary disease have been limited mainly to observations of one particular form of disease in a given family, while for scientific purposes what is wanted is a record of all the diseases, fatal and non-fatal, which have occurred in a given family (*Brit. Med. Jour.* 1888, 11, 287). A beginning of such records has been made in the study of insanity and its relations to chorea, neuralgia, epilepsy, etc.; but they are never complete; and it would require the records of several generations in each of many families to furnish statistical data sufficient to determine the relationships of diseases which are supposed to be connected with what are called gout and rheumatism.

Certain portions of the United States present specially favourable conditions for the study of race influences upon disease and mortality, because different races may be found there under nearly the same conditions as to climate, food, occupation, etc., which is not the case if we attempt to use data derived from countries inhabited mainly each by a different race.

The following table shows for New York City the death-rates per 1000 of the white population during the year ending 31st May 1890, with distinction of birthplaces of mothers and of eight groups of ages. (The birthplace of the mother is the best means at our command for indicating the probable race in this case): —

Birthplace of Mother.	All Ages.								
	All Ages.	Under 15 years.	15 to 20 years.	20 to 25 years.	25 to 35 years.	35 to 45 years.	45 to 55 years.	55 to 65 years.	65 years and over.
United States (white)	29·16	46·92	4·92	7·00	9·67	12·55	20·66	34·41	93·35
England and Wales	27·59	43·28	5·63	10·04	12·96	19·28	29·78	42·70	127·82
Ireland	32·20	43·26	7·75	13·81	20·72	30·76	40·91	63·32	133·11
Scotland	26·55	35·32	4·38	10·77	14·34	20·70	36·21	41·84	108·75
France	24·08	42·46	6·96	5·27	10·22	15·26	28·05	44·31	111·52
Germany	22·08	36·90	4·30	7·73	11·05	16·94	22·65	43·27	84·52
Russia and Poland	21·18	40·25	3·27	4·67	7·01	9·93	20·63	31·25	102·80
Canada	26·85	39·53	5·68	13·24	15·89	28·95	18·25	70·55	95·24
Scandinavia	28·32	62·56	7·72	11·87	14·44	19·21	28·30	49·42	85·23
Hungary	29·25	58·73	7·91	5·49	8·14	11·99	30·84	40·23	102·19
Bohemia	36·22	62·19	5·69	13·11	18·45	20·30	23·54	58·38	89·74
Italy	39·96	84·18	7·94	13·50	11·03	15·36	19·90	38·34	88·40
Other foreign countries	18·06	32·11	4·14	6·39	7·47	13·20	18·96	36·48	66·73

It will be seen from this table that the death-rate of those whose mothers were born in Russia and Poland was very low between the ages of fifteen and forty-five, and that at other groups of ages it was also lower than that of any other race. These people were nearly all Jews, and were 80,235 in number. The death-rate of the offspring of Irish mothers was high, much higher than that of the Germans, and as there were about 400,000 of each of these races, the comparison is a fair one.

The Jewish population was poor, crowded in tenement houses. The interesting point to the medical statistician is, What were the forms of disease to which the marked differences in the death-rates of these races were due? To answer this in part, we will take the statistics of deaths for the six years ending 31st May 1890 for the Irish, the Germans, the Russian and Polish Jews, the American white offspring of American mothers, and the coloured in New York City. The average annual death-rate from consumption per 100,000 of population was—for the Irish, 645·73; for the coloured, 531·35; for the Germans, 328·80; for the American whites, 205·14; and for the Russian Polish Jews, 76·72. The average annual death-rate from pneumonia per 100,000 of population was—for the Irish, 343·99; for the coloured, 389·50; for the American whites, 272·87; for the Germans, 214·12; and for the Russian and Polish Jews, 170·17.

It seems probable that members of the Jewish race possess a distinctly higher degree of immunity against the bacillus of tuberculosis and the micrococcus of pneumonia as compared with the other races above mentioned; and that on the other hand the Irish and the American negro are specially susceptible to the effects of these micro-organisms.

Professor Stokvis has pointed out that in all colonial armies in warm climates the death-rate from diseases of the respiratory organs is more than twice as great among the native troops as it is among the Europeans ("On the Comparative Pathology of Human Races," etc., *Practitioner*, Lond. xlvi. 1891, p. 233), while hepatitis is decidedly more fatal in the European than in the native.

In the Dutch East Indian colonies the natives are decidedly more liable to beriberi than the Europeans; but the comparative immunity of the latter against this disease appears to be decreasing in recent years. Even when we have the means of comparing the death-rates of different races in the same locality it is usually impossible to say how far the differences in these death-rates depend upon inherited peculiarities of physical structure, and how far they are due to the poverty, uncleanliness, and habits as to different kinds of alcoholic drinks which characterise the great mass of the population of certain races.

JOHN S. BILLINGS.

ANTHROPOLOGY AND MEDICINE

Our knowledge on this subject is scanty and far from clear; and the little we believed ourselves to possess has been disturbed by recent changes in pathological theory. Divers diseases formerly supposed to be the outcome of constitutional and hereditary proclivity are now believed to be the results of infection; and the remoter causes are apt to be neglected in the consideration of ætiology.

That many pathological processes are known to be common to mankind and to other mammalia, or even to animals further removed from us, while others are reasonably suspected to be so, makes it *à priori* improbable that any great differences should subsist in the distribution of diseases among different races of men. On the other hand, though men and women respectively can hardly be said to have any peculiar and exclusive diseases (except in so far as this results from the differences in their sexual organs), yet we see that their respective liability to some at least of these diseases varies. A curious instance of this is afforded by cretinism and goitre: goitre being much more common in women than in men, while cretinism is pretty evenly distributed — if anything there is a preponderance of male cretins.

The most conspicuous difference in the external aspect of men and of races of men is in colour; and here comparative pathology would lead one to look for some corresponding differences in susceptibility to disease, for the experience of horse-breeders and veterinarians is pretty clearly expressed on this point. Thus Youatt says that the dark chestnut, as a rule, yields to no other colour in any quality; but that the light chestnut, which appears to be the analogue of the sanguine-blond man, is spirited, but irritable and delicate in constitution. Black horses, again, number among them some of the very finest of their species; but many of them are heavy and dull in temperament, and there is an idea afloat that they are particularly liable to malignant disease. Here we may be led to think of the choleric and the melancholic temperaments. Among breeds of sheep, the blackfaced have the reputation of being hardier than the whitefaced. Certain black pigs, according to Darwin, can eat with impunity what would be poisonous to white ones on the same pasture; and like differences are seen in black and white rats. On the whole, however, the deposition of pigment in the skin and hair of mammals would seem to be the result of processes which connote or accompany health and vigour rather than the opposite.

The statistics of morbidity and mortality, which alone could yield a sound foundation for generalisations on this subject, are unfortunately imperfect, or altogether wanting, in the regions where the material would be most valuable — those regions, namely, where nations of different

colours and constitutions of body live side by side under comparable conditions. In fact, we have hardly any trustworthy statistics, except from the most civilised of the countries, whose populations are compounded from more or less distinct divisions of the human race [*vide* Dr. Billings' art. on "Med. Statistics"].

Much information, more or less trustworthy, as to the distribution of disease among different races, may be gleaned from Hirsch, Lombard, Boudin, Oesterlen, Bordier, etc.; but even where the facts can be relied on, they are generally capable of interpretations that make them of little value for our purpose. Thus, when we learn that aneurysm is four times more common in San Francisco among foreigners than among native Americans, we must remember that a far larger proportion of the foreigners are males in the prime of life, and that most of the hard bodily labour is performed by foreigners.

Negroes are said to be exempt, or nearly so, from piles and from varicose veins, and the cause assigned is the greater strength, in them, of the walls of the blood-vessels. Apoplexy, on the other hand (using the word in the ordinary sense), appears to have no racial preferences. Thus, in New Orleans negroes and whites are said to die of apoplexy in the proportions respectively of 103 and 91. Within Europe — England, Scotland, Prussia and Italy yield almost exactly the same figures for death by apoplexy: in all of them these vary between 10 and 11 per 10,000 living; Switzerland and Holland yield 8·5 and 7·9, but Ireland only 5·9. The deaths from brain disease of all kinds, as returned, are singularly few in the insular parts of Scotland and in the Highlands, where the inhabitants are in blood very near akin to the Irish, so that here one might have supposed one had lighted on a real case of hereditary exemption, or at least favourable hereditary constitution; but the fact that Shetland, where the race is Norse, returns fewer deaths from brain disease than even the Highlands and the other islands, is sufficient to negative the idea that the Gaelic race has any such special immunity. The rate of mortality from this class of diseases is certainly lower in quiet rural districts than amid the hurry and worry or excesses of towns, and this may account for some degree of the apparent immunity; the remainder must be attributed to the tendency to set down all cases of death in advanced life to simple "old age." In Shetland and the Hebrides about 25 per cent of the deaths are thus certified.

In cancer, again, the enormous differences in mortality reports are doubtless largely due to the non-recognition of internal growths. But the differences reported to exist in divers registration districts in England seem too great to be wholly due to this cause, and the extreme variations in both directions are by no means such as would have been expected on such a hypothesis. For example, rural districts in general seem to suffer quite as much as cities, and ancient cities more than great centres of industry, even allowing for the difference of constitution of the population in respect of age [*vide* Mr. Haviland's art. on "Med. Geography of Great Britain"].

There is some little ground for considering cancer to be a disease of civilisation, or of civilised communities and races, though here of course the question of failure in diagnosis comes in with double force. The most formidable death-rates that we have, such as 990 per million living in Drontheim and 930 in Lombardy, come from highly-civilised communities. Cancer is said to be rife in China, but rare in Egypt, the scene of a yet older civilisation. It is thought to be uncommon in the negro race generally, whereas we have seen that it is prevalent in Norway, among one of the blondest populations in the world. The asserted rarity in Iceland may perhaps be remanded for further evidence; could it be proved, it would be of great importance, the Norwegians and Icelanders being of the same race. That the disease is strongly hereditary scarcely any one doubts; and I shall presently submit some evidence to show that in Britain it is especially common among people of dark complexion.

Gout is another strongly hereditary disease, common in certain races and communities, but very rare, perhaps non-existent, in others. Roughly speaking, it is a disease of the ruling races and the higher classes; of the civilised man, not of the savage; of the white man, not of the negro; of cold and temperate rather than of hot climates. Probably there exist large communities of men among whom it never occurs; but, given some of the requisite exciting causes, habitual but not extreme excess in eating and drinking, disproportionate use of the brain as compared with the muscles, consumption of certain kinds of drinking-water, etc., it could doubtless be produced in any race and in almost any climate. Negroes, as I have said, are generally free; but Lobengula, the famous king of the Matabele, drank much beer, and suffered severely. The reported distribution of the disease is very instructive. Thus, in India, it is said, the Hindus scarcely ever suffer; the Mussulmans, freer in diet, sometimes. Gout occurs in China, where the mandarin class unite most of the requisite factors. In Madagascar, the comparatively clever and light-complexioned ruling race, the Hovas, suffer from it; the subject negroes are not known to be attacked. In the United States of America it occurs in the cities, but is little known elsewhere; the American farmer is active and temperate.

The registered death-rate from gout in England is about 25 per million living, in Scotland it is 4·3 per million, in Queensland, where much more fresh meat is eaten than in England, about 5. The chief missing factor is probably beer; but at least we are justified in saying that in these cases differences of regimen and climate reduce the mortality in the same race to about one-fifth.

Still, it must be acknowledged that the distribution of gout has a racial aspect. In France, according to Hirsch, Lorraine, Normandy and Lyons are said to be its chief pasture-grounds: others add Burgundy and blame the wine. The natives of all these districts have more or less of the Germanic element in them. In Spain, the least Iberian of Spaniards, the Asturians, are the most gouty. The Belgians, the Dutch,

the Danes, the Northern Germans, the Upper Austrians, and, in Russia, the upper classes of St. Petersburg and the Baltic provinces (Germans again) are all said to suffer from it. If there be one thing which all these people have in common, it is that fondness for heavy feeding which has been a characteristic of our own most gouty nation from time immemorial, and belongs particularly to the true Saxon-English type.

Phthisis has always been a sort of battle-ground for the believers in infection, and the believers in hereditary transmission and the susceptibility of particular types. Until quite recently, though the former opinion ruled in Southern Europe, the latter was almost universally held in England. And though even now clinical and practical experience point in the same direction as formerly, the general and geographical history of the disease seem to support the infective theory. The effects of local conditions of soil and climate, though undoubtedly very powerful, are not always distinct, and may be used in support of either theory.

The local statistics of phthisis are of very great interest, and could not, of course, be dealt with satisfactorily within the compass of this essay. Some of them seem to point to the applicability to phthisis of the "virgin soil" doctrine, which at first sight seems incompatible with that of the importance of heredity.

Among the more important points which may be taken as established are—

1. The extreme rarity of phthisis at very high elevations.

2. Its rarity in high latitudes: for example, in Iceland.

3. That some of Mr. Haviland's conclusions as to local mortality are correct—for example, that damp clayey soil coincides with a high phthisical death-rate;[1] and that the warm, fertile, ferruginous-red-sandstone tracts of country are most remarkable for low death-rates; "a sheltered position and a warm, fertile soil, well drained, being coincident, as a rule, throughout England and Wales, with a low mortality from phthisis."

4. That, among bodily characters, tall stature is the most distinctly unfavourable.

The following opinions may be put forward more doubtfully:—

1. That though local situation, varieties of social habit, occupation, and the like, overbear and obscure in Britain anything like racial tendency, it would appear that the Gaelic and Kymric or Ibero-Keltic stocks are, cæteris paribus, rather more subject to phthisis than the Saxon and Scandinavian. (The principal objection to this statement is furnished by the very unfavourable position of Suffolk, one of the most purely Anglian counties.)

2. That the tropical negro is particularly subject to phthisis, at least when removed from his own country. The Melanesians, or Oriental or Pacific negroes may be here included; these are the people, incorrectly

[1] Bowditch and Buchanan.

called Polynesians, who work in the Australian sugar-fields, and though well fed and fairly lodged, die of consumption in very large proportions —

PHTHISICAL DEATH-RATE IN QUEENSLAND, 1890 and 1891.

"Polynesians" per 1000 living	16·76
Chinese	1·17
Europeans and Colonials	·98[1]

It is needless to cite statistics of the decimation of the true African negro in other climates than his own. In some cases the figures are even more appalling than those I have quoted from Queensland; and in some of the countries into which negroes have been introduced they seem to melt away chiefly from this cause. The most remarkable exception to the rule is that furnished by the southern portion of the United States of America. Here, though within the temperate zone, a negro peasantry has been firmly established, thrives and multiplies. It is even said that the death-rate from phthisis in the Southern States generally is lower among the blacks than the whites.[2] If it be so it is because the former are the peasantry, and a fairly well fed and lodged peasantry, with a wholesome amount of bodily labour; whereas the whites are generally inhabitants of towns and villages, with inferior conditions of life, quoad liability to phthisis.

The mortality from this disease waxes and wanes in different countries in a manner that invites speculation on the causes of change. England and Holland used to be thought its special seats. But now for a considerable time phthisis has appeared to be on the wane in England,[3] and the death-roll therefrom in the cities of France and Germany and Northern Italy has been growing or becoming more visibly formidable. It has also grown in Scotland coincidently with the growth of urban population, and with what has been regarded as improvement in the dwellings of the rural population. In North Germany the western provinces yield heavier rates than the eastern; and here too, though some might rely upon the racial difference between the true German and the Slav, I believe the real difference to consist in a rather more elaborate civilisation, which brings with it air tight houses and other fair-seeming but really evil conditions.

Yellow fever is one of the most selective and fastidious of diseases; almost as much so as the sweating sickness of the Middle Ages, which on its first appearance is said to have sought out the well-to-do and lusty Englishman, abroad as well as at home, and let the starveling and the foreigner go scatheless. In New Orleans, for example, there is said to be a regular scale of exemption, complete in the case of the full-blooded

[1] Blakeney, *Vital Statistics of Queensland*.

[2] But see article "Statistics."

[3] Partly, no doubt, from a change of name, but not, I think, wholly so. The great increase of deaths registered under bronchitis and pneumonia has been at other ages than those at which phthisis has decreased.

negro, less in the mulatto or other man of colour, less still in the dark-complexioned creole of Spanish or French descent; while even the Southern European suffers less than the Englishman, and the Scandinavian fares worst of all. This sounds a little too artificial; but all agree that the dark skin connotes a kind of acclimatisation to the scourge similar to that which long residence confers. We have here, perhaps, the most conspicuous instance of race peculiarity in disease, the hereditary anomalies of pigmentation in the negro being clearly connected with his exemption from a disease in which that function is much implicated. The yellow colour of the fat in the negro, and the comparative whiteness of the stools, should be remembered in this connection.

Scarlatina is much milder and less formidable in Southern than in Northern Europe. More than one reason suggests itself for this; but the greater frequency of enlarged tonsils in the lymphatic temperament, which is so common in North-western Europe, supplies one of these.

Small-pox is exceedingly fatal to peoples among whom it is introduced for the first time. No doubt this is partly owing to terror at the appearance of a new and dreadful enemy, and to ignorance of proper methods of treatment, etc.; but we can hardly doubt that it is also connected with the fact that any such organism flourishes best in a virgin soil. The frightful amount of destruction of life by small-pox among the North American Indians, especially on its first introduction, can hardly be accounted for in any other way. Thus the Mandan nation was almost destroyed; it has even been stated that in their principal village only forty out of 2000 survived the invasion; but it has never been asserted, so far as I am aware, that with vaccination and proper care the Indians suffer more from small-pox than other races. To show that other races suffer almost equally under similar conditions, we may quote the earliest epidemic of small-pox in Iceland, when 18,000 out of 52,000 were said to have perished. Some facts of this sort might lead one to suspect that past diseases may exercise some kind of protective power against others, even when their relation is much more distant than that of vaccinia to variola. Thus we hear of the discovery of a village church in Tellemarken (Norway), whose very existence had been forgotten, the entire population of its remote parish having, there is reason to believe, been swept off by the black death. In this case, probably, the soil was virgin to many other diseases besides this particular pest: or is it that a population which has not been sifted through the meshes of other zymotics is more vulnerable than another, though apparently more healthy?

Whether the virgin soil hypothesis be necessary to explain the occasional destructiveness of measles may be doubted. Though on its introduction to Fiji it killed about a fourth of the population, it is said not to have been extraordinarily severe among those Fijians who were carefully nursed in European fashion, and protected from their own

folly; the mortality has been quite as great in France under bad sanitary conditions. There is no sufficient reason to think that any one race is more liable to be severely handled by measles than another, under equal conditions. Negroes suffer much more than whites, it is said, in the United States; but the difference is only what we find in this country between the upper and the lower classes. Tetanus and trismus neonatorum are supposed to be particularly fatal among negroes; but here again it is probably the habits of the race that are in fault, rather than anything in its physical constitution. One can hardly imagine any resemblance in the latter respect between negroes and Icelanders; yet the inhabitants of the Westmann Islands, off the coast of Iceland, used to lose the greater part of their infants from trismus, until they were taught by Schleisner to reform their manner of treating them during the first few days of life. Hirsch assigns as a probable cause a peculiar sensitiveness of the negro skin; but the suggestion appears to me unwarranted and gratuitous.

Chorea is said to be unknown in China, and we may probably assume with safety that it is rare. Whatever its relations with rheumatism, it is certainly a disease of the nervous temperament especially. For its physical type see further on. There are several more or less obscure diseases to which negroes seem to be exclusively or particularly liable. Of these is the sleeping-sickness, described in this work by Dr. Manson. The mysterious ainhum, which resembles a limited leprosy, is not known to attack other races; but yaws certainly does.

Of all white races, the Jews are the most likely to reward a careful study of special morbid tendencies; but I am not aware that this has ever been thoroughly carried out. They are known to have a lower death-rate, wherever it has been tested, than the Christian populations among whom they live; but this may be due simply to their sober habits and carefulness in diet, their avoidance of violent labour, and their great care of their children. They are believed to suffer much from diabetes, from nervous diseases, and from psoriasis.

If we now regard the subject from a geographical point of view, we shall be able to make use of the gigantic series of anthropologico-medical statistics which we owe to Dr. Baxter and to the American civil war. Perhaps the clearest and most important fact that comes out of them is the inferiority of the blond-complexioned man for recruiting purposes. Out of twenty-two principal classes of physical defects, twenty of which imply disease of some kind, in only one, chronic rheumatism, did the dark-complexioned recruits yield the larger percentage of rejections. As De Candolle says, the very uniformity of the thing is somewhat suspicious. He suggests that it may be largely if not wholly due to the inclusion of great numbers of Germans, the German emigrants being often of inferior physical type. Other possible sources of fallacy suggest themselves to me; but it must be allowed that a primâ facie case was made out against the blonds. The excess of blonds was most marked in the rejections for phthisis, and for dis-

eases of the circulatory and urinary systems. Dr. Baxter says there was an excess of dark men among the few rejections which took place on account of certain acute diseases. To this point we will return presently.

I have made out a list from Baxter's data, showing in relative order what appeared to be the weakest points in recruits of several nationalities and races: —

1. White men born in the United States were frequently rejected for diseases of the digestive and urinary systems, for bad teeth, and for phthisis.
2. American Indians for *nothing;* they were the soundest of all the nationalities, as well as the tallest and largest in girth.
3. Negroes — For urinary diseases. Also very healthy; but were probably picked men.
4. British Americans — For nothing specially; generally very healthy.
5. Mexicans — Diseases of the nervous and cutaneous systems, syphilis, diseases of the locomotive and generative systems, and local injuries.
6. South Americans — Syphilis and respiratory disease.
7. West Indians — Urinary disease.
8. Englishmen — For bad teeth, and for affections of the digestive organs.
9. Scotland — Diseases of the circulatory, urinary and digestive systems.
10. Ireland — Diseases of the circulatory system, of the skin, and of the digestive system; syphilis.
11. Wales — Phthisis, and diseases of the urinary and locomotive systems.
12. France — Diseases of the skin and the nervous system; bad teeth.
13. Holland — Phthisis; diseases of the skin, eye and ear, and of the respiratory and locomotive systems; and local injuries.
14. Germany — Phthisis; diseases of the circulatory and locomotive systems, of the ear, and of the digestive system.
15. Sweden — No morbid peculiarity; very healthy.
16. Norway — Diseases of the ear and of the locomotive system.
17. Denmark — Diseases of the eye.
18. Switzerland — Diseases of the urinary system; defects of the teeth, of the ear, and of the digestive system.
19. Portugal — Hernia; diseases of the digestive and generative systems.
20. Italy — Diseases of the skin and of the generative system; syphilis.
21. Russia — Diseases of the eye, of the nervous, circulatory and generative systems.
22. Hungary — Diseases of the digestive and nervous systems, of the ear, of the generative and respiratory systems; hernia and phthisis.
23. Poland — Diseases of the eye, and of the circulatory and respiratory systems; phthisis, and local injuries.
24. Spain — Diseases of the respiratory organs; syphilis, hernia; diseases of the generative and digestive systems, and of the eye.[1]

This list, like the results of most voluminous collections of statistics, is after all a little disappointing. It is not easy to draw any important

[1] The numbers examined were small in the cases of the Indians, Mexicans, South Americans, Spaniards, Portuguese, Russians, Hungarians, and Poles.

general conclusions from it except perhaps this, that the native and naturalised races of North America stand better than the recently imported. Thus the red-skins, the aborigines, stand best; and nearly as well stand the West Indians, the coloured men of the States, and the British Americans — mostly, I suppose, French Canadians, — a hardy, unsophisticated peasantry, largely crossed with Indian blood.

Respiratory disease is found rife among Spaniards and South Americans, but not, as might have been expected, among Mexicans, West Indians or Portuguese. The numbers were perhaps insufficient, except in the case of the West Indians.

Dr. Baxter makes a remark on a certain relation, signs of which appear in some of his tables, though not in my abstract of them. It is a sort of general resemblance in the nosology of the British races, among whom, I think, he means to include the American whites, as compared with the other races observed. He found the proportion of rejections to increase with age and with height. To some small extent the latter fact was due to the former one, but the increase of phthisis with a stature beyond 65 inches was far too great to be accounted for in that way. The same may be affirmed of cardiac disease and varix, both of which appear to increase rapidly with increase of stature. Hernia, however, contrary to the opinion of Boudin, does so very little, or not at all. General debility, as a cause of exemption from service, decidedly lessens with increase of stature.

In all these there is a distinct, though not very great excess of men of light complexion. There are, however, a number of morbid conditions entailing rejections, the majority of the sufferers wherefrom are set down as dark, though none of these are of great importance numerically. Most notable are dropsy, cancerous and other tumours, cataract, certain defects or affections of the nervous system — as imbecility, neuralgia, chorea — chronic alcoholism, chronic pleurisy, and certain affections of the portal system, as liver disease, hæmorrhoids and prolapsus. It may be noted that most of these are precisely the vices of the "melancholic temperament."

Next in value, for our purposes, to the great American statistics are those of the French recruiting service; not so much for their intrinsic importance as for the light thrown upon them by Boudin and Broca, and by the investigations of Topinard into the distribution of complexions, and by those of Collignon into that of head-form in that country. Moreover, great as is the assimilative power of the French nation, its principal anthropological types — the Kymric, the Keltic, the Mediterranean, the Norman, etc. — still remain tolerably distinct.

French anthropologists generally take the view that the Norman and the Kymric types are but varieties of one, — the tall, blond, long-headed North European type; and that this, so far at least as it appears in France, is characterised not only by these three qualities, but also by tendency to chest disease, to dental caries, to varices, and to some other affections, from all of which the short, thick-set, dark, round-headed Kelt

of the central provinces is comparatively free. The southern and south-western portions of the country are occupied partly by the last-mentioned race, but partly by short, dark, long-headed people, often classed together for convenience as the Mediterranean or Iberian race; but probably capable of analysis into more than one type or stock, not to speak of various admixtures added during the historic period. We should therefore have in the French recruiting statistics an opportunity almost unequalled of testing the comparative morbidity of different types of man, and the nature of hereditary morbid tendencies, could we rely on the carefulness of the medical examination of recruits. Unfortunately, however, there is intrinsic evidence that, during the period for which we have published statistics, this used to be by no means sufficiently careful and systematic.

For example, it was the practice usually to measure the conscripts, and reject those under size, before investigating the other possible disqualifications. Of course this plan, otherwise unobjectionable, had, from the medico-statistical point of view, the disadvantage that the infirmities of the undersized men were not disclosed or tabulated, and that those departments which yielded a large proportion of small men did not exhibit in the reports their actual proportion of myopia, chest disease, and so forth, but only the proportions occurring in the taller men. But sometimes this order seems to have been reversed, with the effect of assigning to the department or commune under examination too high a stature, but its full proportion of infirmities. These things must be borne in mind in the examination of the table which I have constructed in order to exhibit the relative morbidities of several groups of departments, selected on anthropological grounds. The column headed, "Do., probable, corrected," is the result of an attempt to neutralise the errors resulting from these defects of method. Though conjectural, I have no doubt it comes much nearer to the truth than the official statement. Boudin's book was published when France had eighty-six departments; she subsequently gained three, and then again lost other three, so that the number is once more eighty-six. In forming my table I have always taken the several departments in what may be called the order of excellence; thus, under the column of "Dolichokephaly" No. 1 would be the department with *most* long-headed men; under that of "Mortality" No. 1 would be the department with the *lowest* death-rate, No. 86 that with the highest; under that of "Myopia" No. 1 would be the department with the *fewest* short-sighted youths, and so forth. In making my groups I have thrown together the ordinal figures belonging to several departments, and set down the average in the table. Thus, in the case of the ten departments yielding the tallest men (or rather the fewest undersized men), I set down 5. But the order in which they produce tall men is slightly different from that in which they are free from dwarfs, so that the average position of these same ten, in that column, comes out as low as 12.

Bertillon's order of mortality also requires explanation. Instead of

assessing the mortality simply on the aggregate population of all ages, Bertillon calculated the death-rate for each of twelve age-periods on the population living at such ages respectively, and averaged the several orders thus obtained in order to get the proper rank of the department. The result is sometimes a startling change in its position. Thus the Seine-et-Marne stands fifty-fifth on the ordinary plan, with a death-rate of 23·5. This low position is really owing to the great number of children sent out from Paris to be nursed in this neighbouring department, who sustain a frightful mortality. The ultimate rank of the Seine-et-Marne, on Bertillon's plan, would be the twenty-third; the average of its several ranks, which I have chosen for use in my table, being 29. The Seine-et-Oise similarly leaps from the sixty-fifth to the fortieth place, with an average rank of 41. Indre, where the infant mortality is low, falls from tenth to fiftieth, with average 49, and Creuse from sixth to fifty-first, with 50.

The table (p. 32) is full of instruction, and yields, on examination, some valuable and unexpected results, of a nature not directly germane to our inquiries. Thus, the very pregnant fact comes out that high mortality and military inefficiency — or unsound health from the recruiting-officer's point of view — stand in no direct relation to each other: in truth the relation is very frequently inverse. Thus, of all my fifteen categories the Breton departments stand worst in regard to mortality, but best by far in point of soundness; while the ten thinly-peopled low-country departments have the worst rate of exemption for unsoundness, but, with one exception, the lowest rate of mortality.

The most promising lines of investigation for us, however, are those afforded by pulmonary disease (including especially phthisis), by mental derangement, by myopia, and by defects of the teeth.

Of these the first, as we have learned already, has some relation to tall stature, and this law is borne out by our table, wherein the departments of highest stature take the forty-eighth rank, but those of lowest stature the thirty-fourth. There appears no evidence that colour, *per se*, has anything to do with the matter; the comparatively blond Lorrainers, for example, standing very well in this as in most other respects, and the dark Provençals very badly. The great towns stand ill, of course; but when we find that the ten departments where the northern dolichokephalic race is most in evidence, and the five of Normandy, and the five which I have selected as best exhibiting the combination of tall stature, long head, and blond complexion,[1] agree in yielding a high average of phthisical recruits, little doubt remains on my mind that we have to do with an affair of race or heredity. This is in some degree confirmed by the Belgian statistics, which exhibit the Flemings and Brabançons as yielding more tall recruits and more cases of phthisis than the Walloons.[2] Here, as in other parts of our subject, cause and effect

[1] Viz., Pas de Calais, Somme, Aisne, Oise, and Calvados, the last only a Norman department. I excluded Nord and Seine Inférieure as having a strongly urban character.

[2] See Vanderkindere's and Houzé's papers on Belgian Anthropology.

TABLE ILLUSTRATIVE OF THE DISTRIBUTION OF DISEASE IN FRANCE CHIEFLY FROM RECRUITING STATISTICS.

Number.		Order for high Statures.	Do. low, do. exemptions.	Dolichokephaly.	Blondness.	Mortality.	Do. (Bertillon).	Do., 0 to 5 years.	Exemptions for: Infirmities.	Do., probable, corrected.	Phthisis and Respiratory Diseases.	Weak Constitution.	Scrofula.	Mental Alienation.	Exemptions for: Hernia.	Myopia.	Epilepsy.	Mutism.	Defective Teeth.
1	10 Departments of highest stature	12	5	49	22	33	32	40	49	41	48	44	29	0	36	38	35	41	57
2	10 Lowest stature.	76	81	35	60	49	57	38	42	52	34	59	40	—	40	27	32	50	31
3	10 Most blond .	23	23	28	5	51	42·5	38	40	37	46	42	40	+	33	34	43	50	53
4	10 Darkest . .	56	46	33	81	50	45	51	35	35	49	35	31	— —	42	50	62	55	45
5	10 Dolicho north'n	18	19	12·6	17	57	42	54	57	51	54	47	42	0	49	48	48	42	71
6	10 Do., southern or western . .	64	60	9	62	48	53	49	42	46	43	51	22	—	60	54	43	45	42
7	10 Brachykephaly	38	35	81	52	40	43	38	41	40	33	47	56	0	41	45	43	59	32
8	9 Auvergnat race	60	71	72	63	60	55	52	30	39	27	43	66	—	20	32	44	58	15
9	5 Normans . .	28	26	20	6	43	35	35	62	59	54	55	40	+	45	50	32	43	73
10	4 Bretons . .	74	71	41	28	69	65	41	6	21	22	17	27	—	3	6	41	41	9
11	5 Remo-Lothringians . .	22	14	61	16	26	25	35	39	30	24	41	46	+	43	46	43	48	48
12	6 Urban . .	34	28	25	42	61	59	55+	49	45	62	45	49	++	51	62	46	29	54
13	5 Tall, dolicho-blond combined	12	13	15	15	45	33	54—	55	47	55	50	40	+	37	36	46	39	73
14	10 Mountaineers .	51	48	58	56	53	50	47	42	43	41	32	48	— —	38	49	41	50	36
15	10 Thinly-peopled low-country .	45	46	34	44	29	35	44	62	60	51	54	48	—	52	43	38	37	50

The materials for this table are derived from Boudin (*Géographie Médicale*, 1857), from Broca, from Topinard (*Anthropologie Générale*, 1885 and *Revue d'Anthropologie*, 1889), and Collignon (*L'Anthropologie*, 1890); and from Bertillon père's *Demographie de la France*, 1875.

The number of departments being eighty-six, the normal or mean position is 43·5.

The urban mortality, especially that from 0 to 5 years, is understated, and that of No. 13 perhaps slightly overstated, by reason of the number of town-born and especially Paris-born infants who die in the country.

In the column "Mental Alienation," 0 represents about the average of France, + an excess, ++ a large excess, — a deficiency, — — a large deficiency of insane persons, as compared with the average. Bordier, quoting Chervier, gives a list of departments in which mental alienation is common, and in which no Norman, and no strongly urban district appears.

are almost inextricably confounded; and, in order to understand the problems, the local history and conditions must be studied. Thus in France —

Of 10	brachykephalic departments, only 1 has more than the average density of population.		
Of 10	Northern dolichokephalic departments	10	have more.
Of 5	Norman	5	,,
Of 4	Breton	4	,,
Of 10	Most blond	9	,,
Of 10	Darkest	3	,,
Of 10	Southern dolichokephalic	2	,,

We in England, with our almost unchequered experience of higher phthisical death-rates in cities than in rural districts, would be inclined to say at once, "Here, in the greater density of population, is the one and sufficient reason for the greater amount of phthisis in the recruits from Flanders and Picardy and Normandy!" This would be too hasty a conclusion. In France, as my table shows, the hard-wrought, ill-fed peasantry of the plains suffer much from phthisis and scrofula. The peasantry of Limburg, the most Germanic province of Belgium, and perhaps the most rural except Luxemburg, stand about the worst in this respect. On the other hand Bretagne, the least phthisical part of France, has, as we have seen, a dense population.

The fact is the tall, long-headed blond population is where it is by reason of its physical and moral qualities; its striving, ambitious, masterful character, which enabled it to occupy the best and most fertile parts of France, leaving the hills and heaths to the dark, short-headed Kelts.

Mental alienation has not the same distribution as phthisis and pulmonary disease, which seem to affect the dark southern or Mediterranean race as much as the fair northern one; sparing only the sturdy, dark, broad-headed people of the centre, and the anomalous Bretons. The number of the insane seems to be large throughout the blond area,[1] where it is probably a race-character; and also, of course, in the districts of the great cities.

It has been affirmed that myopia is structurally connected with dolichokephaly, the deep orbit and the long-axed eyeball going naturally with the long head. A certain amount of evidence has been adduced in support of this idea; and the tall blond race has been saddled, in the minds of some anthropologists, with yet another hereditary defect. The evidence of my table is not conclusive either for or against this view but it certainly does something to render it unlikely. Of the five departments selected as representative of the type, one only, the Aisne, had an excess of myopes; and of the ten most blond departments only two,

[1] I draw this inference from Boudin's figures, vol. ii. 235–7; but they are perhaps hardly sufficiently detailed, though very striking.

viz., Eure and Seine Inférieure. In fact, myopia distinctly belongs to the dark-eyed inhabitants of the south of France, and to those of the cities, with the strange exceptions of Lyons and the urban district of the Nord: Brachykephals have their full share of it.

The subject of defective teeth would, of course, furnish material for a goodly volume. So far as my materials testify, good teeth in France go with short average stature, dark complexions, and, less distinctly, with broad heads. Bad teeth concur with tall stature, and almost as clearly with long heads and blond complexion. Or, to put it in another way, teeth are good in the mountains as a rule, bad in the plains, and especially bad, as Boudin himself remarked, around the mouths of all the great rivers. They are good among the Auvergnats (or central Kelts), and especially so among the Bretons; also in the Catalans of Rousillon, etc.; bad among the northern blond long-heads (including the Normans), and among the Gascons; moderately good among the Ligurians. In all these cases the boundaries are pretty clearly drawn, so as almost irresistibly to suggest that either the hereditary constitution of the several races or kindred, or something in the local (may I say tribal) habits and customs must have to do with the phenomena. For example, the Loire Inférieure was formerly politically a part of Bretagne, but its people were not Bretons in blood and customs. Accordingly the Bretons have a very high mortality and very good teeth; the Nantese, or Lower Loire folk, have a low mortality and very bad teeth. On the other hand the neighbouring department of Mayenne was not Breton politically, but its people are said to resemble the Bretons in character. Accordingly they have a rather high mortality and excellent teeth!

This connection between good teeth and a high death-rate is strange, but unquestionable. Of the ten departments which furnish the fewest exemptions for defective teeth, every one has an excessive mortality, and in most cases, and on the average, a very excessive one. They are all in two masses, viz., 1. Auvergne and Lyonnais; 2. Bretagne with Mayenne. If we seek for dietetic causes of caries, we shall find that the great wine-producing districts, Gironde, Dordogne, Marne, Côte d'Or, as well as the cider-drinking Normandy, are among the worst on the list. But, after all, there is plenty of sour wine in Auvergne and of cider in Bretagne.

On the whole, then, I am disposed to subscribe to the belief of the French anthropologists, that we have here another example of a hereditary and constitutional defect. But it is one which cannot be dated back indefinitely; it must have been developed on French soil. Even now the Scandinavians, the purer-blooded cousins of the northern French, are generally "euodont;" and it is certain that when the Saxons invaded England, and the Franks and Normans Gaul, they were still so. If Harold of Denmark, the conqueror of the Cotentin, had not been a singular exception, he would hardly have been nicknamed Blue-tooth.

In the British Isles we have no such groundwork of statistics to work upon as those on which I have been building from America and

France, and I have little more than personal observation whereto to trust. This, however, is sufficient to enable me to assert that phthisis is not here, as some have supposed, especially prevalent among blonds.[1] The proportions of the several colours of hair and eyes in the sufferers are not very different from those which obtain in the general population. If anything, there is even an excess of black and very dark hair. Some statistics given me by Dr. Edward Liddon of Taunton, from the Brompton Consumption Hospital, are confirmatory of my own. I *think*, however (on this point statistics are unavailable), that hereditary phthisis in the upper ranks often presents itself in a frail blond type with very light hair; and I am sure that a fine transparent skin is a sign of vulnerability. In fact, the typical victim of phthisis is, in my opinion, a tall person with blue eyes, a transparent complexion, and dark hair. Such persons are also more liable to hæmorrhages; it would seem that in them other structures partake of the delicate organisation of the skin.

I have already said, *apropos* of the supposed absence of chorea from the Chinese, that, whatever its connection with rheumatism, it is a disease specially belonging to the nervous temperament. Fatal and severe cases almost always present the signs of that temperament. There is usually something remarkable about the development of pigment; the hair is often coal black, but sometimes extremely light, flaxen, or pale red. Epileptics, cataleptics, ecstatics, thought-readers, clairvoyants are very frequently of one or other of these strongly-contrasted colour-types. Mania seems to occur rather more often in the xanthous type, with chestnut, red or fair hair; but with regard to melancholia the observation of the ancients was undoubtedly correct: it belongs especially to the type which they called melancholic, whose outward signs are tall stature, olive complexion, and straight dark hair.

More than one theory has been advanced as to the physical constitution which furnishes the best seed-bed for cancer. For example, it has been said to be very common in persons with orange-hazel eyes, or with eyes in which the colour is much mixed or broken, in which the general effect on a distant view is green. My own observations have not confirmed this notion. Cancer, in my opinion, is most common in people who have a fairly healthy constitution in other respects. The prevailing complexion, among the subjects of cancer in this country, is dark. Out of sixty-seven such, English and Scotch, I found eight with black or brown-black hair, and thirty-two with dark brown; thirty-four had light, ten neutral, and twenty-three dark eyes. These figures vary from those of the surrounding non-cancerous population very decidedly in the direction of darkness. Dr. Roger Williams, who has also investigated this subject and on a somewhat larger scale, has kindly shown me his figures, which bear out my own conclusion. It will be remembered that Dr. Baxter's American statistics also agree with our own on this point. Of course it does not necessarily follow that cancer is

[1] See analysis of upwards of 1000 cases in *Races of Britain*, pp. 222, 223.

at all more prevalent among generally swarthy than among generally blond nations; nor am I aware of any evidence in favour of such a belief. On the contrary, there is some reason for supposing it to be a disease whose development is favoured by civilisation, comfort and intellectual progress; and these are on the whole most prevalent in the races whom Huxley calls Xanthochroi, although it is the swarthy individuals among them who suffer most.

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ON TEMPERAMENT

TEMPERAMENT is usually understood to denote a certain combination of physical and mental characteristics. Its practical importance is of two kinds; as a guide to the disposition to certain kinds of disease, and as a guide to the disposition to certain lines of conduct: the subject of temperament has been treated accordingly by two classes of writers, medical and philosophical. The two have treated the subject in different ways: the physician has considered chiefly, and often exclusively, the physical aspect of temperament; the psychologist, on the other hand, has regarded temperament as a type of mental character with tendencies to certain forms of emotion, and has neglected the physical side. The doctrine of temperament was originally founded on a physiological basis, and physical conceptions of temperament prevailed till the end of the last century. Kant then took up the subject, and although he made use of terms derived from the character of the blood, his treatment was exclusively psychological. Since the time of Kant the subject of temperament has been treated more fully by psychologists than by physicians, and the popular use of the term shows that the word has now come to mean a certain type of mind rather than a certain type of physical organisation. The comparative neglect of temperament by recent writers on medicine is not surprising. Medical practice has gradually been more and more influenced by the exact methods of modern physiology; thus it is natural that the doctrine of temperament, resting on simple observation of more or less vague characters, should have fallen into disuse. At the present time, although the subject of temperament is specifically mentioned by few, its importance is being

more recognised. The predisposition of certain individuals to certain forms of disease, and the different effects which the same dose of the same drug may have on different individuals, are well-recognised facts which show the importance of what is popularly called "constitution." But though the importance of constitution or temperament is acknowledged, little has yet been done to study the subject on modern methods. Whenever it has been studied, as by Stewart in his book, *Our Temperaments*, the old classification has been adhered to with far from satisfactory results. The importance of temperament is also being more recognised in relation to many problems of practical life — to such questions as the methods of education and the choice of occupation in life. Yet here again little has been done in the scientific study of the subject. The doctrine of temperament falls under the head of individual as opposed to general psychology, under the head of that branch of psychology which deals with the differences which distinguish different minds rather than of that which deals with the laws of mind in general. Individual psychology has been comparatively neglected not only by the older school of psychologists, but also by the recent experimental school; and it is but quite recently that a beginning has been made in the systematic investigation of the mental characters on which a scientific doctrine of temperaments should be based.

In order to establish such a doctrine, it will first be necessary to study more closely, and by more exact methods than hitherto, the physical differences which distinguish different individuals. Much has been done in this way by anthropologists; but their investigations have been carried out chiefly from an ethnological stand-point, and it is probable that their methods will have to be modified to suit the different end in view. A second necessity is the investigation of mental differences by exact methods. This has hitherto been the greatest difficulty in the way of a scientific doctrine; but experimental psychology is now sufficiently advanced not only to show how this may be done, but to have taken some steps in this direction. Up to the present time the most important work on these lines of investigation has been done by Mr. Galton. On the physical side his anthropometrical researches furnish the kind of material which is needed to establish the existence of different groups of physical organisation. He has also made some advance on the mental side. His division of individuals according to the nature of their mental imagery, which has been further developed by Charcot and Binet, is a valuable contribution to individual psychology, and an example of the kind of distinction to be made out. At present the most important work on the mental side is being done by Professor Kraepelin of Heidelberg. He and his school work at the subject from the psychiatrical point of view; and one important division of their work has been the investigation of certain fundamental properties of the mind which are of great importance in the study of temperament. These include the capacity for mental work, the susceptibility to fatigue from mental work, the power of recovery from such fatigue, the extent of

the influence of practice, and the power of concentration of attention. They have also investigated the relations of bodily and mental fatigue, the depth of sleep, and other questions of psychical or psycho-physical capacity. In all these investigations they have found that individual differences occur; and it is in such differences as these, so important in relation to practical life as well as to insanity, that we may hope to find the materials for a new classification. It would be fruitless here to attempt to formulate a new system of temperaments. Such an attempt should only be made on the basis of experience gained in the investigation of physical and mental characters by methods such as those of Galton and Kraepelin.

A few suggestions in this direction may, however, be made. There has been singular unanimity among both medical and philosophical writers in favour of a fourfold division of temperaments. Both Kant and Lotze accepted the old division, while modifying and describing the mental characteristics more fully than had been done before. Wundt has retained the old types, but defines them on the basis of the strength of the emotions, and of the rate at which they change. Thus, in the choleric temperament the emotions are strong and change quickly; in the melancholic, strong but change slowly; in the sanguine, weak and quick; in the phlegmatic, weak and slow. One recent writer goes so far as to say that the fourfold division must be approved "by all who advocate intelligently any theory upon the subject." In spite of this consensus of opinion, it would probably be best to put the older classification on one side, and to start afresh from the beginning.

In one direction, however, it may be well to take advantage of previous methods; the old doctrine had a pathological basis, and it is probable that pathological investigation may give us the clue to a more satisfactory method. It is customary to speak of certain dispositions to disease as diatheses, of which the nervous diathesis and the uric acid diathesis may be given as examples. The exact investigation of the physical and mental characters of these diatheses has yet to be carried out, and probably no more useful contribution to the doctrine of temperament could be made than such an investigation.

Another line of inquiry which might be useful is the study of the different characters of the two sexes, and of various ages. The temperaments of age have been most fully considered by Lotze. He regarded the sanguine as the temperament of childhood; the melancholic, or as he called it, the sentimental, as the temperament of youth; the choleric of manhood, and the phlegmatic of old age. The reaction to disease is known to vary with the different epochs of life, and it is probable that exact investigation of the characteristics of different ages may enable us to define groups of temperament useful both from the pathological and sociological points of view. It would be especially interesting to discover whether the individual who retains in adult life the mental traits which are found to be characteristic of childhood, retains also youthful characteristics in his physical organisation.

Another possible basis for a classification of temperaments is purely psychological. As a working hypothesis at the present time, the customary tripartite division of mind might be accepted, and an endeavour be made to find the physical and mental traits which characterise the three types of Auguste Comte — the man of thought, the man of feeling, and the man of action.

It must be remembered that a satisfactory doctrine of temperaments has not only to be useful in defining the nature of the more special disposition to react in certain ways to disease, but also, and perhaps more essentially, in defining the nature of the disposition to react in certain ways to other and more general features of the environment.

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ON THE LAWS OF INHERITANCE IN DISEASE

We all of us have had two parents, and with the rarest exceptions four grandparents. Most of us have had eight great grandparents, and probably to a large majority no fewer than sixteen persons have stood in the relation of great-great-grandparents. Now since tendencies to individual peculiarities, involving, it may be, liability to special forms of disease, may be transmitted not only from parents and grandparents, but from much more remote ancestors also, it is obvious that their investigation presents us with a very complicated problem. In many instances it is almost hopeless to investigate transmission from individual to individual, and we may arrive at safer conclusions by estimating average prevalence in races, families, or classes of society. It is in this latter

way only that many questions which present themselves, not only to the physician, but to the biologist and to the student of sociology, can be satisfactorily looked at. [*Vide* art. on "Anthropology and Medicine."]

We must, however, in the beginning endeavour to define approximately what we believe to be possible as to hereditary transmission. Without venturing to do more than mention the Weissmann logomachy, which has recently disturbed the creeds of some biologists, I will take permission to avow my belief that with the sperm and germ supplied by parents there may pass to the offspring tendencies to the reproduction of all that these parents had acquired up to the date of the sexual congress. By the term "acquired" is meant all that has been received by modification of vital processes, not what has been imposed or taken away by external violence. Not only, however, may offspring derive from parent cells peculiarities of cell and tissue structure with the proclivities attaching to them, but it is also in a high degree probable, that in some instances parasitic elements or specific poisons may pass directly into the tissues of the embryo. Such parasitism may be absolutely latent in the parent, and may remain so for indefinite periods in the offspring.

We have then an inheritance of structural peculiarities and tendencies which is more or less certain, and in addition to it an inheritance of parasitic germs or of poisons, which is uncertain and in a sense accidental. Respecting this inheritance of specific poisons it is necessary here to premise that what takes place may be contamination in utero rather than inheritance in the more strict sense of the word. The two parents do not stand in an exactly similar relation to their offspring in this matter. The father cannot possibly convey any poison unless it be present in his semen; the mother, on the other hand, is in vital relations with the fœtus for nine months after conception, and may, at any date during that period, convey to it any poison which has meanwhile found its way into her blood. Thus variola cannot possibly be conveyed by the father to the fœtus so as to develop only after the birth of the latter; but the mother may communicate it during any period of her pregnancy up to the last month. The same is the case with syphilis, and possibly with some other specific diseases.

It may be convenient to speak first of the laws of inheritance of these diseases which are caused by specific poisons. Of these the principal, and the one respecting which most is known, is syphilis; and it may be allowed to stand as an illustration of the rest. The facts in our possession make it very probable that when syphilis is derived by a child from a parent, it is conveyed by the actual transference of some specific material, probably of a particulate and organic nature. The child does not inherit any modification of tissues which the parent may have undergone, but takes over specific germs which are destined to multiply in its blood and produce phenomena of similar character and in similar order to those which its parent has previously manifested. This character and this order may be greatly modified, but they will be essentially the same. Thus, however much the health of a parent may have been

damaged by syphilis, he will transmit to his offspring nothing unless the specific virus of the disease be present in his semen, and in those particular spermatozoa which go to the fertilisation of that particular ovum. A man might on this hypothesis beget a syphilitic child one week, and a non-infected one the next; nay, it is even possible that of twins one may receive the poison and the other escape it. It is needful to state this definitely, for although we have as yet no direct proof of this proposition, the hypothesis is necessary to any clear comprehension of the facts.

The following are the facts which appear to have been established respecting the inheritance of syphilis: —

That the father may infect his offspring (the mother having never suffered in any degree), and that this is by far the most frequent mode by which the taint is transmitted.

That the mother may infect her offspring, and that she may do this not only at the time of conception, but at any period during pregnancy, up to within the last few weeks.

That there is much uncertainty whether a child will or will not receive the poison of syphilis when born of parents one or both of whom are tainted. Thus a child may wholly escape under circumstances apparently the most dangerous.

That the nearer the conception to the date of primary disease, in one or both parents, the greater the risk to the child.

That in the tertiary stage a parent may suffer severely and yet have healthy offspring.

That the severity of the disease in the child is in no relation to that shown by the parent — many of the worst instances occurring in children of parents who were apparently in good health. Severity in the child is therefore probably, as in the adult, a matter of idiosyncrasy in the recipient, and not of peculiarity as to source.

Of twins one may suffer and the other escape.

Although it is the rule for the first-born after the parental acquisition to suffer and for younger ones to escape, yet now and then remarkable exceptions to the rule may occur.

That with rare exceptions, the period during which a parent retains the poison of syphilis in a transmissible state is limited. In the father it rarely exceeds two years, but as regards the mother nothing trustworthy can be stated.

Although in the case of syphilis no one has yet succeeded in recognising the specific germ which is its cause, whilst in tuberculosis this is supposed to have been accomplished, yet the fact respecting contagion and inheritance remains far more vague and uncertain in the latter than in the former malady. When a disease may be obtained by contagion unwittingly and very easily — its germs possibly being almost omnipresent — it becomes very difficult to prove anything as to inheritance. Thus there are not wanting those who, relying too exclusively upon modern doctrines of bacillary causation, and supporting their creed by

so-called statistics, are disposed to deny altogether the effect of inheritance in tuberculosis. In the investigation of this important question, we must not restrict ourselves to the narrow platform of tubercular disease of the lungs. We must comprise all the various maladies with which we now associate the tubercle bacillus, and take in all forms of bone, joint, and gland scrofula, with also the various affections of the eye and the skin (lupus and its allies) which are in such association. If in this way we take cognisance of the whole domain of scrofula and tuberculosis, it is, I think, impossible for any one acquainted with the facts to disbelieve in the power of hereditary transmission, and rest only on the theory of contagion from without. The subject is one much too complicated to be well suited for illustration by statistical calculations; these are as likely to mislead as to help us.

Two factors are admittedly of great importance in reference to the development of tubercular affections: we must take cognisance not only of the bacillus itself, but also of the state of the tissues upon which it is implanted. The possibilities of inheritance are therefore twofold. It may be that the bacillus itself may pass bodily or potentially with the sperm or germ from parent to child, or it may be that a condition of tissues liable to its attacks, but for the time free from its presence, may be the result of transmission. If we are permitted to name the tissue-condition, which is prone to favour the development of the tubercle bacillus, the name "scrofula" will perhaps be convenient for the present. A child may then inherit "scrofula" without the bacillus, or the bacillus without "scrofula"; or, what probably is most common, both may be present together. Pathological facts leave us in no doubt that the tubercle bacillus may find its way into the body of the fœtus in utero and may there develop. Whether it does so in association with the semen, or in union with the maternal germ; or whether it is always derived by the ovum from the mother's blood, we are as yet uninformed. We may plausibly conjecture that any one of these three modes is an easy possibility. The life history of the tubercle bacillus is probably by no means wholly known to us. We do not know, for instance, what are the conditions or how long the periods under and during which it may remain latent in the tissues. Many clinical facts suggest that it may in some resting form be present in most persons — waiting until some local damage or some degradation of general health gives it opportunity for development. The prevailing creed which suspects external contagion as the cause of all scrofulous and tuberculous attacks is probably a much too narrow one. It is clear, however, that as regards the heredity of phthisis and scrofula, we can at present do little more than state preliminary facts and suggest possibilities. We are by no means yet in a position to put forward conclusions.

If we turn from tuberculosis to leprosy, a malady which is possibly a congener, we shall encounter similar sources of uncertainty. Yet, if we can get a clear view of the facts, the two will perhaps throw some light on each other. Firstly, a bacillus very like that of tubercle attends

the development of all the most severe forms of leprosy. When leprosy ends fatally it is often by the supervention of pulmonary disease not distinguishable from phthisis. The facts as regards contagion are much the same in the two, and are matters chiefly of conjecture. In both maladies it is certain that almost unlimited opportunities for contagion may occur without any evidence of its accomplishment. Now, until quite recent times, the belief in the hereditary transmission of leprosy has been almost universal. The more careful investigations of modern observers have, however, thrown much doubt upon this creed. It is quite certain that the children of lepers, born out of leper districts — in England or the United States for example — never inherit it. The occurrence of the disease in the children of lepers in a leprosy district is no evidence at all; for obviously they have been exposed to the endemic cause whatever that may be. If it be, after all, a food disease, they may have partaken of the tainted substance. The recent inquiries of the Leprosy Commission in India, which collected facts at the Schools for the Children of Lepers, pointed to the conclusion that there is no proof of heredity, since these children did not manifest the disease in greater proportion than others. The very prolonged periods during which leprosy may remain absolutely latent (ten years or more) introduces, however, an element of uncertainty into all these investigations. We may safely believe that in the case of leprosy the influence of heredity is a very small factor, but it would be unwise to deny its possibility.

If we turn now to the consideration of maladies which are induced, not by any specific virus, but by the inheritance of anatomical or physiological peculiarities, a few general propositions may be ventured.

There is probably no peculiarity, whether of structure, of function, or both, which can be acquired or augmented during the life of the individual which may not be reproduced in his or her offspring; yet the transmission of such peculiarities is by no means a matter of certainty: one child may suffer and another escape. Of this uncertainty double parentage is probably the chief explanation.

It is quite possible for an individual in whom any given tendency derived from a parent may never have disclosed itself to transmit such tendency. Thus a disorder or peculiarity present in a grandfather may be revealed in his grandchild just as special features in the countenance or other resemblances may be transmitted. It is possible, indeed, that a peculiarity of structure leading to derangement of function may be transmitted through many generations, and yet show itself in very few individuals in each. Under some law, as yet not well understood, it is possible for a peculiarity of structure to show itself suddenly in several children of the same parents, there being no proof of its previous occurrence in the progenitors. To this group of maladies the term family diseases has been given; but it must be clearly understood that it refers to the members of one single family and not to descendants in several generations.

Illustrations of the wide topic upon which we now enter occur on every side. The inability to digest the albumen of eggs and of milk

which is often met with as an idiosyncrasy in related individuals in several generations must depend upon the constitution of the gastric juice, which in its turn is due to some peculiarity in the glandular apparatus of the stomach. It may serve as an example of a thousand other peculiarities, some more and some less well marked. To the whole group we give the name idiosyncrasies; and although we leave them for the most part unexplained they are none the less real, and dependent no doubt upon actual structural aberrations. Very often a sufferer knows that some predecessor — grandparent or great-grandparent — had the same peculiarity. Were habits of family observation and record more cultivated, no doubt such evidence would be still more frequently forthcoming.

Psoriasis does not very often affect several brothers and sisters, but it frequently seems to be transmitted from parent or grandparent. Thus it may persist through many generations, but still affect but very few individuals. Its subjects are almost always in good health, and the balance of evidence as to its nature would incline us to suspect that it depends upon an inherited peculiarity of the structure of the skin.

The laws of inheritance come to our aid in explanation of many of the peculiarities presented by exceptional diseases of the skin; and these in turn illustrate the laws of inheritance in a very instructive manner. Inherited peculiarities in structure must be invoked to explain such phenomena as excessive tendency to freckle; the liability to blister in the sun, proneness to chilblains, liability to urticaria and pruritus. It is for the most part those who have inherited a skin in which the sebaceous glands are large who become the subjects of comedonous acne.

Amongst the "family diseases" which chiefly show themselves on the skin we have the common forms of xeroderma or ichthyosis; and the rare malady known as Kaposi's disease, or xeroderma pigmentosum. In ichthyosis almost invariably one-half of the family of children suffer whilst the others wholly escape. Evidence of it is often but not always present at birth. There appears to be no regard to sex. The same statements are true of Kaposi's malady, which consists of a most excessive tendency to the formation of freckles, which are apt to run into ulceration. Its occurrence reveals a congenital imperfection in the structure of the skin, which renders it unable to withstand the irritation of ordinary sunlight. In this feature it has much in common with retinitis pigmentosa, a disease occurring often in several members of one family, and due to degenerative changes in the retina apparently induced by exposure to light.

The tendency to bleed on slight cause, which constitutes the "hæmorrhagic diathesis," affords us another good example of a family disease. It is, however, not one of those which is restricted to a single generation, being almost always an heirloom, and with the peculiarity that it manifests itself almost exclusively in the male sex. It is quite possible that our inferences on this latter point may be somewhat exaggerated, for the menstrual relief in women not improbably prevents other

forms of hæmorrhage, and in families in which the males are bleeders menstruation in the women is often profuse. The proved relationship of hæmophilia to inherited gout leads to the consideration of the latter malady itself in reference to inheritance. This is a topic which requires much patient attention to detail for its clear apprehension. It is not a simple matter: we must not restrict our conception of gout to attacks of acute podagra, but must include in the term all the conditions which lead up to such attacks, or can be proved to be in association with them. By general consent the liability to gout is hereditary; indeed it may even be doubted whether in its more typical forms it is ever acquired in a single generation. That the gouty state may be induced by luxurious living and defective exercise is a proposition which no one will deny; that it can be so induced with equal facility in all persons is, however, well known not to be the case. In some very slight errors in self-management will cause it; whilst in others no excess, however long continued, seems to be sufficient. The difference as we observe it under the existing conditions of society is probably in the main a difference in the strength of inheritance, though at the same time it may be true that certain differences in race, family, and temperament may in the first instance have made themselves felt. Of the middle classes of society in England, and amongst other communities where gout has been long prevalent, it may be held that all inherit the tendency more or less remotely. If we attempt to explain in what that tendency consists, we must begin by saying that in the first place it consists in peculiarities of appetite and digestion, and next in defects in the excretory organs. The man who inherits gout inherits peculiarities of stomach and kidneys, and of all organs which are concerned in the assimilation of food and the depuration of the blood. We may take this as perhaps the simplest expression of the inheritance of gout; but there must follow on it the assertion that he inherits also peculiarities of various other kinds. His cartilages and ligaments, his nerves, his muscles, his blood-vessels, in fact every tissue in his body, has acquired some modification, and with it some special proclivity to disease. Congestions, inflammations, nerve pains, whatever may have been their exciting causes, will in him assume a special character and lead to specialised results. Thus the offspring of generations of gouty ancestry may, in virtue of such descent, suffer from various maladies which stand in no direct relation with errors in diet, defective assimilation, or the accumulation of urates in the blood. One of these is the weakening of blood-vessels, which is the proximate cause of hæmophilia, and may also find its expression in epistaxis, hæmorrhagic purpura, bleeding into the vitreous, and other phenomena. In the same way inherited gout may be the parent of iritis in early life, and of various forms of joint disease at all periods of life, which are wholly unassociated with the deposit of urate of soda in the structures. It is an inheritance of tissue proclivity independently of, though usually in addition to, peculiarities of assimilation and excretion. Nor must it be forgotten that these inherited liabilities may have been inextricably

mixed with others. Feebleness of circulation, instability of nerve function, scrofula, and other causes of disease, may have joined with inheritance of gout, and the resulting state may thus be a very complicated one.

It is not necessary to say more than a few words respecting the heredity of congenital defects in the growth of *external parts*. It is universally admitted that such defects as coloboma iridis, harelip, superfluous digits, webbed digits, and the like may be and commonly are hereditary. We also observe respecting them that occasionally they occur in many members of the same family; whilst there is little or no evidence as to their occurrence in former generations. This has been especially noted in certain instances of harelip and defects in the iris, and it is especially of interest in reference to the explanation of other forms of "family disease."

Another important law which receives occasional illustration in these very obvious hereditary defects is that of "transmutation in transmission." By this expression is meant that the defect reproduced is not always exactly the same as that in the predecessor. Thus one child may have a superfluous digit, and another of the same family merely a deformed and overgrown one. What is hereditary is clearly a liability to disturbance in the development of a certain portion of protoplasm, but falls short of the necessary production of identity of result. This law is probably of wide application under conditions in which it is not so easy to prove its influence. In the case of various forms of skin disease it may be conjectured that a liability to defective formation of the skin in general is the antecedent rather than a definite proclivity to one single type of malady. Thus an inheritance from a parent who has suffered from psoriasis may possibly be transmitted as ichthyosis, or some form of chronic eczema or lichen. Many of the known facts as regards "family diseases" support the belief that some law of unity in variety influences their production.

JONATHAN HUTCHINSON.

MEDICAL GEOGRAPHY OF GREAT BRITAIN

THAT branch of medicine which has for its subject the Geographical Distribution of Disease, may be said to have had a very remote origin in the ancient Coan School of Medicine, of which the family of Hippocrates were the founders. In this school the study first sprang into existence as far as we can judge, and then flourished for a time under the care of the author of *Airs, Places, and Waters*, the head of the above distinguished family, whose genius, common-sense, and vast experience, extending over an unusually long life of active practice among the isles of the Greek Archipelago, and the mainland

of Greece, Thrace, and the Coast of Asia Minor, enabled him to accumulate a vast number of clinical facts bearing upon the relation between certain classes of disease and certain conditions of soil, water, and atmosphere. Within the circumference of his wide experience he had almost every variety of land-surface from the Mount Olympus to the paludal lakes of the plain, and the swamps alongside the river mouth; over those lands he noted the sweep of the atmospheric currents, the different lie and aspects of their slopes towards wind and sun. Of the winds he studied their moisture, dryness, and temperature, and attributed the excess or defect of these qualities to their courses over the neighbouring lands and seas. The different effects of the various waters on mankind — the hard, the soft, the brackish, and paludal — were also noted by Hippocrates, and locally the effects of weather and seasons were also studied by him, whether in his reports of clinical cases, or of epidemics (1).

In the etiology of disease Hippocrates evidently foresaw the great importance of the physical configuration of the land, its aspects and soils, and the influence of the two great factors of local climates, the sun and the atmosphere, — the latter ever varying in its currents, temperature, moisture, and adventitious constituents, whether of mechanical, vegetable, or animal origin. The later results of the study of medical geography justify these early anticipations of that great physician.

Since the death of Hippocrates (B.C. 480–357) the subject stood still until the publication by Dr. Alexander Keith Johnston of his well-known *Physical Atlas of Natural Phenomena* (2), in which maps appeared of the geographical distribution of certain diseases. The data were gathered principally from the works of our naval, military, and mercantile marine medical officers and others, within whose stores of facts there are many that might still be profitably studied.

In 1856 the eminent French physician and medical geographer, Boudin, published his *Géographie Médicale*, based principally on the statistics of the French army — the first statistics used in the study of medical geography. In this work France was divided into *departments*, each so shaded as to indicate death-rates, or the number of conscripts rejected on account of certain diseases in proportion to the populations.

In England the data for constructing maps of disease distribution were not published in serviceable form until the late Dr. William Farr issued his Decennial Supplement for 1851–1860 to the Registrar-General's (Major Graham) 25th Annual Report in the year 1864. Dr. Farr published two supplements, including the decennial periods 1851–1860 and 1861–1870, giving the number of deaths from twenty-five different causes at certain age-periods, among males and females separately, for each of the 630 registration districts during each of these ten years; since then the present Registrar-General has confused the sexes and rendered his supplement for 1871–1880 useless for this branch of study.

The history of disease distribution is fully dealt with in my recently published work (3); I will now give the salient facts resulting from my own investigations from the year 1868 up to the present time.

The first firm step in the study of the medical geography of Great Britain was made within a short time of the publication by Dr. William Farr, C.B., of the supplement already referred to. In this important and model report the deaths from twenty-four different causes during the ten years 1851–1860, in each of the 630 registration districts of England and Wales, were arranged in two tables, one for *males* and one for *females* respectively. The mean populations of each sex in each district were divided into so many (17) age-periods, giving (1) the mean number of males and females living during the decennium at each age-period; and (2) the number of deaths from each of the twenty-four causes during the same time at each of the said age-periods: thus the death-rate from each cause at each age-period could be calculated — the mean populations at the different ages being given in the same column as the actual number of deaths from the different causes. With the life and death statistics so arranged the medical geography of England and Wales, and the construction of maps showing the geographical distribution of each cause of death in the 630 districts, became possible for the first time in the annals of medicine; and future investigations into the causes of the varieties of the several distributions, as well as of the marked inequality of the distribution of each individual cause of death, found a solid basis. Such a map once constructed and coloured in varying shades, enables the student at once to compare it with other maps of the geology, physical geography, hydrography, meteorology, etc., of the country under observation; and lastly, with other maps of the distribution of other diseases over the same area, and of the distribution of the yield of such crops as wheat, a plant whose habits and peculiar construction I have shown to be remarkable exponents of local climates.

In 1875, whilst my first folio edition was going through the press, the Registrar-General of Scotland issued his Supplement to the Annual Reports for the ten years 1861–1870, which contained a summary of the deaths in each of the thirty-three counties during that period from heart disease, phthisis, and cancer: he did not, however, take the precaution of separating the sexes, or of giving the number of deaths and the mean populations at each age-period. It enabled me, however, to extend my inquiries and to construct sketch maps, although very imperfect ones, of the distribution of the above causes of death in that part of Great Britain.

I will now give an outline of what has been achieved in the medical geography of England and Wales.

Heart Disease. — The first map constructed was that of the geographical distribution of heart disease and dropsy during 1851–1860, amongst a mean population of 18,996,916, or 9,278,742 males and 9,718,174 females, distributed over 630 registration districts, amongst

whom had occurred 236,973 deaths from this cause, of whom 109,527 were males and 127,446 females.

As the annual death-rates from this cause were found to differ only as 11·8 (males) to 13·1 (females), a careful study of the death-rates of the two sexes in each district was made: the difference in the mortality attributable to sex was found too small to necessitate two maps, especially as the organ affected was common to both. The map, therefore, represented the deaths of both sexes, namely, 236,973, or nearly a quarter of a million, and at all ages. The districts having a mortality from heart disease *above* the average of the whole country (12·0 to every 10,000 living) were coloured in shades of *blue*, the *darkest blue* representing the *highest* mortality; and those having death-rates *below* the average were coloured *red* in different shades, the *darkest red* representing the *lowest* mortality.

A map was constructed and coloured in accordance with the above scale, which ranged from 4–6 — the lowest rate — to 19–21, the highest annual death-rates to every 10,000 males and females living in each registration district during the ten years 1851–1860.

The Map of Heart Disease. — When a map of the 630 districts in England and Wales is coloured on such a scale, and each separate district coloured with a shade of blue or red according to its death-rate, it will be found that instead of the map presenting the appearance of a "crazy-patch work," it will be characterised, according to the disease chartographed, by groups of red and blue districts, which suggest at once to the observer that some unknown general condition gives a certain measure of uniformity to the forms and positions of the groups he sees before him.

The observer must now compare the disease-map, and its remarkable groups of *high* and *low* mortality, with a good map of the physical geography of the same country — such as that constructed by the late Sir A. C. Ramsay (Stanford) — and carefully note each physical feature represented on it with each group of high and low mortality. This will prove an easier task than at first it appears to be, for every country, even the smallest islands, have their water-partings and river-catchment basins, their ridges of high ground, and their valleys in the lower, through which the rivers and their tributaries take their courses to the ocean or some inland sea. Throughout Great Britain these river-catchment basins have been well defined on excellent maps which help the student at every step of his investigation. In the case of heart disease the first glance at the two maps will disclose the following remarkable coincidences: — (1) The east coast of England and the west coast of Wales — in fact, those parts of the country most exposed to the force of the sea-winds — are characterised by almost continuous groups of low mortality, red. (2) Wherever on the physical map the outlets and courses of the large rivers are seen to have their axes corresponding in direction with the prevailing winds — such as the south-west and north-east — groups of low mortality are observed on

the disease-map invariably to extend far into the country, as in the cases of the Tyne, the Tees, the Humber, the Norfolk and Suffolk rivers, the Thames, the Severn and Avon, the Welsh rivers, the Mersey, the Westmorland and Cumberland rivers. On the other hand, (3) wherever the trends or axes of the rivers are more or less at such angles to the courses of the prevailing winds as to preclude their free access, and force them to blow over their valleys instead of sweeping up through them, there on the disease-map we see groups of high mortality (blue). In the latter instance the river valley systems are imperfectly air-flushed, as in Hampshire, Dorsetshire, Devonshire, Herefordshire, and other districts where the axes of the rivers are opposed to perfect ventilation by the prevailing and other winds.

The exceptions to the littoral groups of low mortality are found to be in those districts characterised on the physical map by high precipitous and rock-bound coasts, which protect the land to the leeward, and thus offer barriers to air-flushing. Coincident with these conditions are groups of districts of high mortality (blue), as in Northumberland, the North Riding, Somersetshire, and Devonshire. With these facts before us we begin to understand the importance of the characters of the foreshores of a country; for in studying the two maps in detail, district by district, we are constantly meeting with the coincidences of flat foreshores and low mortality, and precipitous foreshores and high mortality, which are in harmony with the low mortality of the well-flushed valleys and the high mortality of those imperfectly ventilated.

Since the above results were obtained I have visited all the highest mortality districts, and found that great prevalence of endemic rheumatism in one form or other coincided with the heavy death-rates from heart disease. I have also mapped out the data for 1861–1870, and found that the distribution of *high* and *low* mortality groups during the second corresponds with those of the first decennium. During the ten years 1861–1870 the mean population amounted to 10,417,596 males and 10,971,649 females, of whom died from heart disease 136,531 males, and 151,916 females, equal to a total mortality of 288,447, which added to the mortality from this cause during the first period, brings the total mortality to more than half a million deaths spread over twenty years (525,420), and enables us to formulate the proposition: (*a*) That throughout England and Wales *low* mortality from heart disease is found in all those districts where the valley-systems are open to the free air-flushing by the prevailing and other sea-winds; and on the other hand *high* mortality is found in all those districts with protected valley-systems, the river courses of which are at such angles as to preclude free air-flushing, and to force the winds to blow *over* instead of *up through* them. Such unventilated valleys are equivalent to the "*stuffy hollows*" which the experience of Hippocrates taught him to denounce, and which, as I found by another investigation even in such a fertile county as Devon, were incapable of producing a wheat-yield above twenty-one bushels per acre, the average for England and Wales being twenty-nine bushels.

We now proceed to the medical geography of a totally different cause of death — cancer; and as this disease is twice as prevalent among females as among males, we shall confine ourselves to its distribution amongst that sex.

Cancer. — During the ten years 1851–1860, amongst the female population above stated (9,718,714), there occurred throughout England and Wales 42,137 deaths at all ages from this cause, — a death-rate equal to 4·33 to every 10,000 females living; whereas amongst the male population (9,278,742) there occurred only 18,059 deaths at all ages, equal to an annual death-rate of 1·94 to every 10,000 living, or less than half that for the other sex. The scale represents the usual six degrees of mortality, those above the average in shades of *blue*, and those *below* in shades of *red*, representing different annual death-rates — the *lowest* between 1–2 to every 10,000 living (*darkest red*), and the *highest* 6–7 (*darkest blue*). The scale for deaths among females at and above thirty-five years of age ranged for the same period from below 10 to 18 and upwards.

A map of the 630 registration districts of England and Wales so coloured according to the mortality at all ages, or at and above thirty-five years of age, presents certain well-defined groups of *high* (blue) and *low* (red) mortality as in the case of heart disease, but differs from this in certain important features.

If we place such a map by the side of the one of physical geography, we shall find that the highest mortality groups cluster around the lower courses of fully-formed rivers that seasonally flood their riparial districts, from the Tweed to the Thames on the east coast, and from the Stour to the Tamar on the south, whilst along the west coast of England and Wales, with the exception of the districts watered by the North Devon Taw, the Severn, the Dee, and the Eden, *low* mortality predominates. On the east coast we see the lower courses of the Tweed, the Tyne, the Swale, the Derwent, the Humber, the Witham, the Ouse, the Yare, the Stour, and the Thames, all characterised by groups of high mortality. We see similar groups surrounding the lesser rivers of the south coast; and among the rivers emptying themselves into the Bristol Channel we have the notable examples of the Severn and Avon marked by groups of high death-rates, and farther north the rivers Dee and Eden. So far the map of physical geography will aid us up to a certain point as regard the high mortality groups; but when we proceed to discuss those of *low* mortality we find that we must have recourse to a geological map of England and Wales, such as Greenhough's, although in the final stages of our work we must study each district and each parish separately side by side with the maps of the Geological Survey. For this purpose the Sanitary County Diagrams, on a 4-miles to the inch scale, are very useful, especially as an index map of the geology of Great Britain is being published by the Geological Survey on the same scale. On comparing the low mortality groups of districts with the same areas in the geological and physical maps, we

shall find that they correspond with the most elevated tracts of country — tracts where floods are rare or temporary; in fact, the lowest mortality groups follow the courses of the water-partings, whilst the highest, as we have seen, are to be found in the lowest and most frequently flooded valleys. The geological map further informs us that the areas covered by the lowest mortality groups correspond with areas of the older rocks, such as the Cambrian, Silurian, and Mountain Limestone; whereas the highest mortality areas are coincident with the more recent formations, especially when they consist of *clays*, such as the Oxford, Lias, Gault, Wealden, London, and the still more recent alluvial.

We are therefore able to summarise the above facts in this proposition: that the cancer fields in England and Wales are found in the sheltered and low lying vales, traversed by fully formed and seasonally flooded rivers, and composed of the more recent argillaceous formations; and that the districts having the lowest death-rates from this cause occupy the more elevated areas composed of the oldest rocks, amongst which the *limestone* areas are coincident with the very *lowest* mortality.

Phthisis among Females. — In studying the distribution of phthisis we shall again have recourse to the map of physical geography. We have now to deal with populations having in their midst an indefinite number of individuals bearing in their lungs the bacillus tuberculosis of Koch. In every district there are males and females acting as hosts to this parasite; and clinical observation tells us that such individuals are at all times liable to fatal disease when exposed to certain persistent causes of irritation and subsequent inflammation of the lung tissue in the neighbourhood of the parasitic colonies. Amongst these are sudden chills from exposure to cold when heated, or to more protracted chills from dampness of clothing. But there is another source of irritation of the delicate mucous membrane of the lungs ending too frequently in inflammation and suppuration of the lung tissue, namely, exposure to the force of strong winds from the sea. We all know the almost instantaneous effects of exposure to such winds even among the healthiest and strongest, as evidenced by watering of the eyes and running at the nose, signs of temporary catarrh, which too frequently extends to the lungs, and there, in the consumptive, arouses the fatal activity of the hitherto dormant tubercle bacillus.

Now of the 9,718,174 females who lived during the ten years 1851–1860 more than a quarter of a million died from phthisis pulmonalis (269,618), — the scale of six degrees ranging from 17–20, the *lowest* (darkest *red*), to 37–40, the highest (darkest *blue*).

Remembering what the heart disease map taught as to the effect of the prevailing sea-winds blowing up through and air-flushing the valleys lying in this direction, we shall have no difficulty in recognising the areas most exposed to the force of the sea-winds; and on the contrary, those other areas that are so shut in by barriers to their free access as to form unventilated hollows, in which those with damaged lungs find protection from their force and other qualities of

the sea gales which render them injurious to lungs which are either morbidly sensitive or already invaded by the bacillus of Koch. Thus along the coast of the eastern counties, and far inland from the low foreshores, we observe a large and important group of high mortality districts. This area in the heart disease map is characterised by an equally large group of low death-rates. Again, along the coast of Wales, up to its central ridge or back-bone, is another large group of very high mortality which corresponds to the large group of *low* mortality from heart disease. Again, along with the low-lying north-western foreshore and far inland — an area well exposed to the sea-winds, especially to those from the north-west — and that which on the heart disease map showed a low mortality, is, however, in this phthisis map coloured in the darker shades of blue, indicating a very high mortality from the latter cause. On the other hand, the low mortality groups of phthisis are to be found on the leeward side of the Welsh back-bone where the air is purest, but robbed of its *force*, which had been broken on the windward side of the mountains where the highest mortality prevailed. Again, if we study the low mortality groups along the north-east coast of Yorkshire and Northumberland, we shall find that these areas are protected by the precipitous cliffs of the coast lines from the full force of the sea-winds. If we now take the protected Thames valley, where so much rheumatism, heart disease, and cancer prevail, we shall find another large group of low mortality from phthisis, notwithstanding the dampness of the climate arising from clays and floods.

If we now compare the phthisis and cancer maps, we shall become aware of the strong contrast that one bears to the other. As a rule where high mortality groups (*blue*) are found in the one, low mortality groups (*red*) are seen in the other, and *vice versa;* this arises from the fact that cancer prevails in the deep, low-lying, well-protected river-valleys, where the force of the sea-winds is mitigated. If we now examine the low mortality groups of cancer we shall find them on the high, dry Palæozoic and much exposed formations, where phthisis prevails.

The propositions as regards the distribution of heart disease, cancer, and phthisis, laid down for England and Wales are equally applicable to those causes of death in North Britain.

The benefits to be derived from this study, which is far too vast to be adequately handled within the space of this article, are of a two-fold character. To the medical practitioner the maps are guides in his consulting room, which enable him to avoid recommending places unfit for the relief of the several diseases under discussion. With such maps before him he would hardly recommend a member of a cancerous family to reside in a low-lying, oft-flooded argillaceous district; or of a phthisical family to take up his abode where he would be exposed to the full force of strong sea-winds; or a rheumatic person with threatened heart affection to continue living in the stuffy, unventilated hollows first described by Hippocrates.

Secondly, the maps will direct the bacteriologist to the localities where the several diseases prevail, and to the soils that seem to favour or to repress the vitality and distribution of pathogenic parasites. We have yet to discover the microbe that determines the rheumatism which ends in heart disease, and seems to be scattered by air-flushing winds, and accumulated in the supra-soil atmosphere of pent-up valleys.

ALFRED HAVILAND.

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A. H.

INFLAMMATION[1]

PART I. — A GENERAL SURVEY OF THE PROCESS OF INFLAMMATION

CHAPTER 1. Introduction. — CHAPTER 2. The Comparative Pathology of Inflammation. — CHAPTER 3. The Main Forms of the Process of Acute Inflammation in the Higher Animals.

PART II. — THE FACTORS IN THE INFLAMMATORY PROCESS

CHAPTER 1. On the Part played by the Leucocytes. — CHAPTER 2. On the Inflammatory Exudation. — CHAPTER 3. On the Part played by the Blood-Vessels. — CHAPTER 4. On the Passage of Corpuscles out of the Vessels. — CHAPTER 5. On the Part played by the Nervous System. — CHAPTER 6. On the Part played by the Cells of the Tissue. — CHAPTER 7. On Fibrous Hyperplasia and its Relationship to Inflammation.

PART III

CHAPTER 1. On Classification. — CHAPTER 2. On Systemic Changes accompanying Local Injury and Inflammation. — CHAPTER 3. Conclusion. — BIBLIOGRAPHY.

PART I. — A GENERAL SURVEY OF THE PROCESS OF INFLAMMATION

CHAPTER 1. — INTRODUCTION

Definition of Inflammation. — It is usual to begin the description of a morbid process by defining that process. In the case of inflamma-

[1] The following article is an attempt to bring into order the very numerous recent researches upon the inflammatory process, and to show whither they appear to tend; it pretends in no wise to be a complete treatise upon the development of our knowledge of the subject. Space alone has forbidden that I should trace the full history. I would therefore strongly urge that as a corrective other works be consulted in which the earlier theories are treated at length; more especially would I recommend (as throwing light upon the progress of our knowledge) Professor Burdon-Sanderson's article upon Inflammation in Holmes's *System of Surgery*.

tion, however, we have to deal with a process so complex, so modified by modifications of the many factors involved, and so variable in its manifestations according to the variety of its causes and the region of incidence, that the attempt to define it has proved a pitfall to pathologist after pathologist; moreover, to advance a definition of the process at the beginning of this article in terms differing to any considerable extent from those employed by previous writers, would demand a criticism of the many previous attempts; and in order that the definition put forward be duly supported, would necessitate an essay covering the whole field about to be traversed. I shall then leave definition to the end, until I have marshalled my facts, and have brought into line all that appears to me necessary for a correct understanding of the process. The definition must be the summing up of the subject, not the introduction thereto.

Use of the Name. — Yet, in the meantime, inasmuch as divergent views are held of the limitations of the use of the name inflammation, a few words of introduction are advisable.

Two courses are before us: either to employ the name strictly in accordance with the primitive definition, and thus only to include as cases of inflammation those states in which there are present redness, swelling, heat and pain, rigidly excluding all cases in which these cardinal symptoms are not present; or, on the other hand, departing from tradition, to include as inflammations all those morbid processes which seem to have a cause and progress inseparable from and merging into the cause and progress of the state characterised by the classical symptoms. The first course is impossible; it is as though one were to declare that red phosphorus is not phosphorus because in externals generally it does not agree with the definition of the yellow form made years before the allotropic modification was discovered. We are now well agreed that of the classical symptoms, one, two or three may be unrecognisable, and in fact absent; and yet the condition of inflammation be undoubtedly present.[1]

The second is the only possible course, that, namely, which associates all those states which under suitable conditions may result in the production of the four classical symptoms, and moreover originate from a common cause. Holding this view, it will in the meantime be well for me, in order to afford a starting-point for the description and discussion of the subject, to select from the many definitions one which is based not on symptomatology, but upon ætiology, and indicates a common origin for all cases of inflammation. I would select that which in this country has received the most cordial support, the definition given by Professor Burdon-Sanderson in his well-known article in Holmes's *System of Surgery*: "The process of inflammation is the succession of changes

[1] A course allied to this has found favour of late years among sundry surgical pathologists, who would limit the use of the term to those cases and those only in which the classical symptoms, or the majority thereof, are present and associated with suppuration,— they urge with Hüter that inflammation only occurs when pyogenic micro-organisms are present, and state that when a wound heals aseptically it heals without inflammation. This modified course is equally impossible; pyogenesis must not be confounded with inflammation

which occurs in a living tissue when it is injured, provided that the injury is not of such a degree as at once to destroy its structure and vitality." This definition includes too much. The hæmorrhage that occurs in the liver when it is injured, and the changes that there occur in the extravasated red corpuscles, are scarcely to be classed among inflammatory phenomena; the atrophic changes which occur in the retina, when through injury it becomes detached, are due mainly to malposition and disuse rather than to the primary trauma. But, as Dr. Burdon Sanderson has pointed out, the definition has this great advantage, that stating the cause, it clearly recognises inflammation as a process and not as a state. The external manifestations of this process under favourable conditions — where the region injured is a loose and vascular tissue, and where the injury is sufficiently severe or extensive — are redness, swelling, and heat with pain: redness from the congestion of the vessels; swelling from the exudation of fluid and corpuscles from the congested vessels; heat from the increased amount of blood in the region, and pain from the pressure upon and irritation of the terminations of the nerves in the region. To these four symptoms may be added a fifth, disturbance of function brought about by this departure from the normal condition of the region. Under unfavourable conditions — where the region injured is dense or less vascular, or where the injury is less severe — one or all of these symptoms may seem wanting; nevertheless a minute examination of the tissues will show the same succession of changes as in the former case.

Chapter 2. — The Comparative Pathology of Inflammation

Accepting, then, this working definition, in order to arrive at a due comprehension of the succession of changes which we take to constitute the inflammatory process, it will be well with Metschnikoff[1] to institute a series of observations upon the reaction to injury exhibited throughout the animal kingdom from the lowest forms upwards to man. By this means we shall be enabled to determine what factors in the inflammatory process are from their constancy of primary importance; what are common and essential, and what are superadded in the higher animals.

The Response to Injury among the Protozoa. — Beginning our study with the lowest and simplest forms of life — forms so lowly that they have been regarded both as animals and as plants — we find even here phenomena accompanying the reaction to injury which throw light upon the inflammatory process as seen in the higher animals. Taking as an example the amœba, we find, in the first place, that the nucleus plays an

[1] The succeeding paragraphs are of necessity very largely an epitome of sundry portions of M. Metschnikoff's most pregnant work upon the comparative pathology of inflammation. By comparing them with the work in question, it will, however, be seen that they depart from it in several points; more especially in dwelling upon the extracellular activity of the wandering cells, and in bringing more prominently forward the response to injury on the part of the fixed cells.

important part in this reaction. If, as Metschnikoff has shown, one of the larger amœbæ be cut in two, the region of injury becomes rapidly indistinguishable — the protoplasm of each moiety closes up, leaving no mark or scar: but of the two parts that which retains the nucleus grows and proliferates; the other disintegrates in a longer or shorter time. Or injury may induce changes in the protoplasm of the entire amœba: thus, Miss Greenwood points out that, without necessarily bringing about death, the interrupted current or an aqueous solution of thymol leads to a process of exudation or extrusion of clear hyaline spheres, or of spheres holding crystals and granules, from the surface of the organism — a process resembling that occasionally seen in the cells of an inflammatory area in higher animals. Nor is this all; apart from changes in the structure of these unicellular animals, differences may be seen in the behaviour of amœbæ towards foreign bodies. It would seem, according to Le Dantéc, that amœbæ ingest non-irritating foreign substances indifferently, provided they be sufficiently small. Around each particle so ingested a vacuole is formed, and the fluid in this becomes increasingly acid, and at the same time digestive. Krukenberg, Reinke and Miss Greenwood have conclusively proved these and similar food vacuoles in the amœba and other Protozoa to contain a pepsine or digestive ferment, which, as Le Dantéc has shown by very delicate tests, exerts its action in an acid medium (the general protoplasm of the cell body being alkaline); this digestive process leads to the solution of food stuffs, preparing them to be taken up by the protoplasm of the organism. If the foreign substances be incapable of digestion they are sooner or later extruded. It is by this formation of digestive vacuoles that the amœba acts upon and destroys bacteria, diatoms, and other microbes ingested by it. There are, however, microbic forms around which it would seem that no proper vacuolation is developed, or if developed, the acid digestive fluid is neutralised by substances discharged from the parasites; where this is the case, instead of destruction there is continuance of vitality and actual multiplication of the invading or parasitic form, leading to the eventual death of the amœba. Metschnikoff has observed this chain of events in one of the amœbæ which ingests and becomes the host of a minute rounded form, the Microsphæra. Phenomena of like nature may be observed among the ciliate and flagellate infusoria. While these phenomena may primarily be regarded as the method employed by the Protozoa for the assimilation of food stuffs, they also are clearly the means whereby the Protozoa defend themselves against living organisms which have gained entrance into them, and thus form the reaction to possible injury; for when in certain cases the means of defence are overcome, the parasitic organisms gain the upper hand and lead to death.

There is yet another reaction to injurious influences exhibited by the Protozoa into which it is necessary that I should enter at some length. This is exhibited by the amœba, but can be and has been most fully investigated in the myxomycetes — multicellular forms which

can with equal propriety be classed as animals or plants, although usually they are included among the latter. These organisms form large plasmodia (masses of protoplasm, that is), in which, under ordinary conditions, the nuclei are the only indication of the individual cells which by their fusion have formed the masses. They are to be met with in leaf mould, and on the surface of moist decaying wood over which they creep with an amœboid movement; and inasmuch as they may attain great size — some species attaining twelve inches or more in length — they form admirable material for biological study.

Ten years ago Stahl, investigating one of these myxomycetes (the *Æthalium septicum*, an organism found in tan pits), showed that if placed upon a moistened surface close to a drop of infusion of oak bark, the plasmodium moved actively towards and into the infusion; if placed similarly near to a solution of glucose (0·5 per cent) it moved with equal rapidity away, and so also in the case of solutions of various salts. These observations of Stahl were (if we except Engelmann's observations in 1881 upon the tendency of sundry bacteria to remove from regions poor in oxygen to those where oxygen is present in abundance) the first of a series of observations upon the attraction and repulsion of plants and portions of plants by chemical substances. To this property Pfeffer, who has made the fullest series of studies upon it, has given the name of chemiotaxis, in place of Stahl's narrower "trophotropism"; and one speaks of a positive or a negative chemiotaxis according to the attraction or repulsion exerted. If, as Metschnikoff has pointed out, the advancing edge of one of these plasmodia (of Physarum) be injured by cauterisation, the region of injury dies; the protoplasmic currents, which had been advancing, reverse themselves abruptly, and within an hour the plasmodium has moved away, leaving the débris of the destroyed region behind. These experiments are so simple, and the results obtained seem so natural, that it may be asked whether it be worth while to attach a name to this property of living matter. Yet the name is in itself an aid to bearing these properties in mind; and, as will be pointed out later, the recognition of them is of material help in solving certain of the difficulties that present themselves in the study of inflammation in the higher animals. Among these myxomycetes another fact can be made out. Stahl observed that the plasmodium of Fuligo, which at first moves away from a two per cent solution of common salt, will after a time (more especially if it has suffered from lack of water) adapt itself to the solution, advancing its pseudopodia or protoplasmic processes into it. With other myxomycetes the same adaptation has been observed. That is to say, by use or adaptation a negative may be transformed into a positive chemiotaxis. To this change I shall have occasion to revert.

The Response to Injury among the Metazoa. — Passing from the Protozoa to the Metazoa, we reach immediately (or almost immediately) a series of beings in which the division of labour among the cells has led to the development of three cell layers — an outer ectoderm, an inner endoderm, and an intermediate layer of mesoderm.

Even in the very lowest forms among the Metazoa it is noticeable that of these three layers there is one, the mesoderm, whose cells have the especial function of reacting when any irritant or injurious stimulation is applied to the organism. Taking what are perhaps the simplest forms in which to observe the relationship and properties of these layers, Metschnikoff has studied these results of injury in the larval forms of astropecten and other echinoderms. At one well-recognisable stage these larvæ resemble little more than the gastrula stage of the embryologist; the endoderm or hypoblast appears as a cul-de-sac — an invagination of the ectoderm or epiblast — while the mesoderm is represented by amœboid cells, budded off from the endoderm, lying or floating in the semiliquid substance filling the general body cavity. The ectoderm is so delicate that any sharp substance can readily penetrate into the body cavity; and, when this happens, it is noticeable that the wandering mesodermal cells make their way to the foreign body, attach themselves to it, and fuse into plasmodial masses, thus forming a wall, as it were, around the invading substance, and cutting it off from the general body system. Here, then, in an organism possessing neither nervous nor vascular system, the reaction to injury, where that injury has not been sufficiently intense to cause destruction of the outer layer of cells, is simply and solely confined to the wandering cells of the body; there is no effusion of fluid; there is not necessarily phagocytosis on the part of these cells; any digestive and destructive action on their part — any attempt in this way to remove the foreign body — must then be by excretion, *by extracellular action*. At the same time, this fusion of the cells and formation of a plasmodium around foreign substances of greater diameter than the individual mesodermal cells may be looked upon as a mechanism whereby the equivalent of intracellular digestion is gained. But, as among these low forms cases occur in which, without the formation of plasmodia, the cells perform their destructive action upon bodies of larger size than themselves we do not lack examples of what must be considered as excretory destructive powers on their part. That these cells in the echinoderms are also capable of destroying minute foreign bodies by intracellular action, that is, by phagocytosis, has been demonstrated in the larger transparent larval form known as Bipinnaria Asterigera; on introducing bacteria under its ectoderm the mesodermal cells are seen to approach, and by their long pseudopodia to adhere to and ingest the still living motile bacteria, which are rapidly digested.

Besides this reaction to injury on the part of the mesodermal cells, a further response is exhibited to a remarkable degree among the lower Metazoa — I refer to the great power of regeneration of lost parts, of cell proliferation leading to the reproduction of destroyed regions. This power is best seen in the classical example of the Hydra, which may be cut into many pieces, each one of which is capable of growing, so that in a relatively short time it becomes a fully formed individual. It is interesting to note in relation to the frequent tendency towards hyperplasia and excess growth following upon injury in

the higher animals, that among low forms, such as Hydra and Cerianthus, the same tendency is yet more strongly marked. Thus, as Loeb points out, if an incision be made in the stem of a Hydra, a whole new oral pole, provided with tentacles, will branch out from the region of cell destruction. In the actinian Cerianthus the process is not quite so extensive; yet from the lower lip of the lateral incision a set of tentacles develops in all respects similar to those around the mouth.

Ascending to the Worms, we find that the protective agency devolves upon mesodermal cells suspended in the perivisceral fluid, and again forming the peritoneal endothelium. We arrive, that is to say, at a state in which a lymphatic system may be said to be present; for the spaces in which the free corpuscles lie are strictly homologous to the lymph-containing spaces of the vertebrate organism, and these corpuscles may be regarded as lymph corpuscles; the peritoneal endothelium corresponds with the mesodermal peritoneal endothelium of vertebrata.

Among the annelids the process of reaction to injury may be well followed in the earth worm by studying the sequence of changes that occur around the gregarines which infest the male genital organs. While these parasites are active by their movements they prevent the adhesion of the wandering cells; but so soon as they pass into the resting stage antecedent to spore formation, the cells form a thick mass around them. The parasite on its part forms a thick cyst wall; nevertheless, it may not unfrequently be observed that, despite this protection, the parasite changes its appearance under the action of the surrounding plasmodium, and in fact is killed. While this is happening no change could be detected by Metschnikoff in the neighbouring blood-vessels; these appear to remain completely inactive: no exudation is noticeable nor any recognisable change in volume.

While among the Worms a well-developed and closed vascular system is not unfrequently present, in other animal forms, which in most respects present a much more complex and advanced development, namely, in the Arthropods and Tunicates, this is not the case. In these the blood pours from the tubular heart sooner or later into the lacunæ of the general body cavity; and whether veins be absent (as is most usual), or present (as in the Cephalopods), the blood is sucked back from the body cavity into the heart. This incomplete circulation, interesting as it is in connection with the development of the vertebrate circulation, is interesting also from the fact that its incompleteness in these large and wide-spread classes of animals prevents reaction to injury from being associated with vascular changes. The blood in these animals, circulating through the ramifications of the body cavity, is evidently a mesodermal fluid, if it may be so termed. Its corpuscles are clearly mesodermal; and without going into full details as to the properties of these corpuscles, it may be said that they represent an interesting series of stages in the subdivision of labour. For example, as Mr. Hardy has shown us in a low form of crustacean like Daphnia (the

water flea), but one form of cell is present, whereas in the highly-developed Astacus (the cray fish), there are three distinct forms of leucocytes (no red corpuscles being present), each of which appears to have distinct functions. The one form in Daphnia has the property of taking up fat globules and food particles from the alimentary tract, foreign particles, such as granules of carmine or Indian ink, and the spores of parasites (Monospora, Metschnikoff); it is granulated, containing minute spherules which stain with basic aniline dyes (basophile granules), and under certain circumstances it may be seen to explode with lightning-like rapidity. In the higher Astacus there are in the circulating hæmal fluid two varieties of cells: one is extraordinarily explosive; when removed from the body cavity it gives off fine blebs or vesicles of its substance with such rapidity that, unless the greatest care be taken, nothing is seen of the cell save its nucleus; this form is phagocytic: the other form is far more stable, and is loaded with large spherules which have a great affinity for acid dyes — they are eosinophilous — may be actively extruded, and undergo decomposition; these cells never act as phagocytes. The third form, with basophile granules, is rarely found in the blood, and then only as the result of special stimuli; but it is present in considerable numbers in the peculiar tissue which forms a sheath around certain of the arteries — Haeckel's "Zellgewebe;" this form is phagocytic, and can be seen to contain globules of ingested fat.

As Metschnikoff demonstrated, in his most remarkable study upon a disease of Daphnia caused by the entry of the spores of a yeastlike organism (the Monospora) into its body cavity, its one form of leucocyte can be seen to react swiftly towards the spores; the cells approach them, form a plasmodium around and eventually digest and destroy them. If, on the other hand, in consequence of their great numbers or the relative paucity of the leucocytes, certain of the spores be not attacked and develop uninterruptedly into mature torulæ, the leucocytes show no tendency to approach them — in fact, their neighbourhood leads to the explosion of the leucocytes — and the torulæ, multiplying, lead to the death of the organism. Often, again, brown eschars may be recognised upon the transparent carapace of a Daphnia, due to injuries by other individuals; beneath these scars are to be found masses of leucocytes which remain in the region of injury until the cells of the tissue have proliferated, and there is complete union and repair.

In addition, then, to the immediate reparative and protective reaction of the leucocytes, there is exhibited among the higher invertebrata a later reaction in the shape of proliferation of the fixed cells. This proliferation, while not so extensive as among the lower invertebrates, can nevertheless be very great; and cells of all forms, whether of hypo-, meso- or epiblastic origin, and tissues so highly developed as the muscular and nervous, may participate in it. In illustration of the ample power of tissue reproduction after injury possessed by these animals, I need but mention the trite examples of the reproduction of the hinder segments

of divided worms, and in crustaceans the restoration of injured and cast off claws and appendages.

Many more instances might be given to show that the reaction to injury remains essentially a reaction on the part of the wandering and fixed mesoblastic cells of the organism, followed in sundry cases by proliferation of the fixed epi-, meso- and hypoblastic cells, and by repair where these have been destroyed. Although these arthropods, molluscs and tunicates have a vascular system, yet, inasmuch as this is open, its changes, if they occur, could scarcely modify the inflammatory process.

The Response to Injury among the Vertebrata. — If now we pass to the vertebrates, the picture presented is far more complex: not only do these present a highly-developed nervous system, but, moreover, the blood is enclosed in a complete vascular system. We shall now consider at length the results of an injury of an organ in one of these higher animals.

Chapter 3. — The Main Forms of the Process of Acute Inflammation in the Higher Animals

The Experimental Production of Inflammation in Non-Vascular Areas. — Let us begin with the succession of changes that occurs in the simplest case, namely, *in a non-vascular area, in one of the lowest vertebrate forms* — for instance, in the embryonic axoloti ten to fifteen days old; let us curarise it, and apply a minute crystal of silver nitrate to the side of its flattened transparent tail fin, washing away the remains of the crystal with salt solution; or again, we may pass into the tail a small needle filled with finely-powdered carmine. By either procedure a certain number of cells is destroyed. The neighbourhood of the injury now becomes swollen (it may be by imbibition of water through the wound), and the surrounding cells tumefied, vacuolated and less refractile. This is the *first stage* — that of injury and modification of the surrounding tissue. In a little time a few wandering cells (leucocytes) approach the injured region; by the next day these are present in fair numbers, and can be seen to have taken up the particles of carmine or débris of the destroyed tissue. This is the *second stage* — that of immigration of leucocytes. There are no vessels in the transparent fin of these young axolotls, no dilation of those nearest to the fin, and no diapedesis. All the leucocytes that pass to the part are pre-existing wandering cells of the connective tissue, — a fact of some little importance in connection with the origin of certain of the pus cells in the suppurative process of higher animals. The *third stage* is that of repair, of proliferation of the injured epithelium, return of the fixed cells of the tissue to their previous state, and emigration of the wandering cells. A very similar progress of events occurs if the experiment be repeated upon the tail fin of the young newt. The same rapid alteration in the large branched connective tissue cells (which become vacuolated as their

long processes are drawn in and shortened), and the same immigration of motile cells from the surrounding connective tissue are to be seen; but here we now find the earliest evidence of vascular participation, for, according to Metschnikoff, complete arrest of the circulation may occur in the nearest vascular loop. By the next day the parts have returned to the normal condition.

If from these cases we pass to mild inflammatory disturbances affecting the non-vascular regions of animals far higher in the scale, we again discover a like process of events. For this purpose *the cornea* affords an excellent opportunity; in health it is absolutely non-vascular; it is perfectly transparent, and is so thin that it can readily be examined microscopically.

The cornea of mammalia, and indeed of vertebrates in general, is formed of fibres which run in layers parallel to the surface. These fibres, while roughly arranged side by side and parallel to one another in any given layer, are placed at an angle to the fibres of the layers above and below. Although free from blood-vessels the cornea is far from being devoid of channels along which lymph freely passes. Between the several layers there exist spaces in which lie the flattened connective tissue cells of the organ; and, by means of numerous fine channels, these spaces around the cells are connected with similar spaces lying anteriorly, posteriorly and laterally. Through this rich anastomosis of channels there is a free flow of lymph. These channels are really continuations of the body cavity of the animal; they represent, and in fact play the same part as the single body cavity of such a simple form as the larva of Astropecten, while the cells lying in the spaces are mesoblastic cells which have become fixed.

Few studies are better calculated to impress the investigator with a sense of the depth of the well at the bottom of which truth lies, than a research into the abundant literature dealing with observations upon the stages of the inflammatory process as it occurs in the cornea, and with the deductions therefrom. One after another the adherents to successive forms of inflammatory belief have found in experiments upon this simple tissue ample support for their particular creeds.

Selecting from among the many observations those which have stood the test of time, I will begin with the simplest, and pass on to those dealing with an increasing intensity of the inflammatory process.

If, as Senftleben first pointed out, the centre of the cornea of a rabbit be washed with a strong solution of zinc chloride, then, in favourable cases, although the epithelial covering be gravely injured, there may be no actual rupture of the outer layers of the tissue. Such a cornea removed twenty-four hours later may show no sign of migration of leucocytes — no sign, again, of congestion of the vessels at the periphery. The only indications of injury and reaction may be the destruction of the corneal corpuscles immediately beneath the cauterised area, and the appearance of a zone surrounding this in which the corneal corpuscles appear enlarged, distinct and tumefied. The process may

continue and advance insensibly to repair without the intervention of leucocytes; the hypertrophying cells of the "granular" zone eventually undergoing karyokinesis, and thus by multiplication replacing the corpuscles destroyed.

Here, then, necrosis and new growth of the fixed cells of the tissue are the only recognisable factors in the process of repair of injury. It must be confessed that the conditions permitting this simplest form of reaction are of rare occurrence; it is worthy of attention that they can exist.

By a slight modification of the preceding conditions another factor may be brought into play. If, after cauterisation in the manner above described, a break be made into the cauterised surface; or if again, without cauterisation, a little of the corneal tissue be removed, then in a few hours a small whitish opacity is to be noticed within the corneal tissue in the immediate neighbourhood of the break in the continuity, and upon examination this opacity is found to be due to a massing of small round cells. As there is at this moment no sign of proliferation of the connective tissue cells of the cornea, these newly-collected cells can only be leucocytes; and further examination of their properties proves them to be such: there is, however, no evidence of dilation of the peripheral vessels, no indication of diapedesis through their walls. The leucocytes, therefore, can only have entered into the wound from the cornea itself and from the conjunctiva and the lachrymal fluid bathing it. In this experiment the inflammatory process is represented by destruction of tissue and immigration of leucocytes, followed by repair; neither the vascular nor the nervous system play any part in it. We are forced to the conclusion that the leucocytes have massed themselves in the injured area purely on their own initiative; and that there must be an attraction, a chemiotaxis or chemiotropism, leading them actively to approach the region of cell destruction.

The observations made upon these two simple cases help us materially to understand the series of events which occur in more intense inflammation of the cornea, such as that produced by injuring the surface and causing the entrance into the injured region of a small quantity of a pure culture of the Pyococcus aureus. This may be accomplished by injecting the culture into the centre of the healthy cornea by means of the needle of a Pravaz syringe (Jacobs). The micrococci so introduced grow rapidly, the growth so extending along the lymph spaces that a branched mass of the microbes is produced, having the spot of inoculation as centre. Around the growth as it extends may be seen a sharply-marked area in which the corneal corpuscles show evidences of degeneration; the nuclei stain faintly, and the corpuscles, speaking generally, have a shrunken appearance. Here, again, the first effect of a microbic, as of a simple chemical injury, is to bring about degeneration of the fixed cells of the tissue. Within eighteen hours the zone of proliferating cocci and cell degeneration is well marked; and now the second stage begins to be clearly manifest, namely, the determination

of leucocytes to the seat of injury. Within twenty-four hours there is a dense packing of these corpuscles around the central degenerated area, and great numbers of leucocytes may be seen converging along the lymph spaces from the periphery of the cornea. This is the second stage of the process, the first stage of reaction to the injury inflicted by the invading micro-organisms. If, as by Cohnheim[1] in his original experiments upon the injury to the cornea, more careful examination be made into the stages of the determination of leucocytes, it can be seen that this determination is closely related to changes set up in the vessels at the periphery of the cornea; they become more prominent, the region has a congested appearance, the smaller as well as the larger vessels are dilated, and there is abundant evidence that the leucocytes are passing out from the contained blood into the surrounding lymph spaces. Indeed the accumulation of leucocytes shows itself first at the periphery of the cornea near the vessels, and gradually approaches the region of injury. Into the mechanism of this diapedesis, and into a fuller description of the changes that take place in the blood-current in these distended vessels, I shall enter later when discussing the changes in highly vascular regions. Suffice it to say here that no distinction can be made out between the behaviour of the leucocytes in the previous experiment, when they entered the wounded area from the external surface, and in this where the majority find their entrance from the blood; as in the previous case the part played was evidently active, so must it be here also. We cannot arrive at any other conclusion than that some attractive force leads to their determination towards the inflammatory focus. As we can easily show, by repeating the experiment, many of these leucocytes take up and contain numerous cocci, while other cocci remain free in the tissue spaces. Many of the leucocytes degenerate and present a broken down appearance; and, as at the same time an increasing area of the corneal tissue becomes disintegrated, an ulcer appears. According to the virulence of the culture and the reaction on the part of the organism, the process may now extend, a larger and larger portion of the corneal tissue becoming affected; or, on the other hand, there may be an arrest of the progress, the massing of the leucocytes preventing, as a barrier, the further extension of the micrococci into the lymph spaces;[2] while at the same time there is an advance of newly-formed capillary vessels into the previously non-vascular tissue. It is to be noticed that the blood-vessels at the periphery of the cornea are prominent and dilated, and from them fine new vessels with very delicate walls pass towards the injured region. At the same time many of the corneal corpuscles, outside the area of destruction, can by appropriate staining be seen undergoing mitosis and proliferating. Thus the active repair of the tissue is initiated.

[1] There can be no question that Cohnheim in his experiments induced not a simple keratitis but one which in the absence of aseptic precautions rapidly became septic and suppurative.

[2] Into the details of this action I shall enter more fully later.

The Experimental Production of Inflammation in Vascular Areas. — From this study of inflammation, as it occurs in a region devoid of blood-vessels, let us now pass on to the more complicated process of inflammation in vascular areas; and, as in the previous case we considered an ascending or advancing series of reactive changes, so here let us begin with the slightest injury associated with the mildest reaction, and pass onwards to states in which the inflammatory manifestations are more and more pronounced.

If an incision be made with a perfectly aseptic instrument into the skin, also rendered aseptic, and be so made as to divide the dermis and tissues immediately below, without at the same time injuring any large vessel, it is the common experience of modern surgeons that repair takes place with the minimal amount of change recognisable as inflammatory. Repair takes place indeed so rapidly that, if the divided structures have come or have been brought into immediate contact, there may be firm adhesion at the end of twenty-four hours. This is *primary union*, or union by first intention, which, rare in the old days, commonly occurs in this era of aseptic surgery. The full sequence of events in these cases cannot, it is true, be well determined by continuous microscopic examination; but if the rabbit or dog be employed, and tissues, wounded in the manner described, be removed and examined at successive short intervals, we see that the changes which occur are mainly, nay almost entirely, related to the pre-existing cells of the part. The section divides a certain number of capillaries; but in the very act of division the divided walls are apparently brought together; and, partly by this means, partly by contraction, the lumina of these minute vessels become occluded, and the hæmorrhage into the wound is altogether inconsiderable. Within an hour after the operation it is evident to the naked eye of a careful examiner that the immediate neighbourhood of the wound is slightly reddened and tumefied, but only very slightly; and, associated with this, there is a feeble exudation between the apposed surfaces. But the exudation is not great, and even within this first hour after the infliction of the wound there may be development of fibrin and coagulation of the exudate, leading to the formation of a provisional cementing together of the opposed surfaces. In this exudation, and in the tissues in the immediate neighbourhood, the leucocytes that have undergone diapedesis may be few and far between, and may scarcely attract attention. The reaction, then, on the part of the vessels and of the leucocytes is of the slightest. Study of sections shows that the main rôle is played by the pre-existing cells of the part; of these a certain number (not so many as might *à priori* be expected) are destroyed immediately, and show all the signs of disintegration; a number relatively large have been injured only, their nuclei remaining intact, though their processes or some portions of the cell bodies have been cut through. It is difficult to determine these injuries in the small cells of the cutaneous tissues; they are better seen in the peritoneum when slight inflammatory changes have there been

induced. This, however, can be made out that the cells in the immediate neighbourhood of the wound became enlarged, and, without showing signs of division, prolong themselves (that is to say, send out prolongations) into the region of the provisional fibrinous cicatrix. In this way, before the end of the second day, there may be a more or less complete replacement of the primary unorganised cementing substance by organised growing tissue, — formed, in the first place, by the interlacing of processes from the neighbouring cells; in the second, and later, by a multiplication of these cells, together with a development of new capillaries, few in number, which branch off from the slightly-congested vessels in the neighbourhood. Thus in this case the process of repair is characteristically associated with hypertrophy and the new growth of the fixed cells of the tissue; while vascular changes, exudation and leucocytosis, are relatively little marked. I have, however, never come across a case in which they have been entirely absent, save when the section has been truly extra-vascular — that is to say, when it has not penetrated into the vascular region of the skin, and has affected only the epidermis and outermost layers of the dermis. In such cases the response to injury may show itself purely as a proliferation of the epithelial cells.

As I have said, observations of the above nature labour under the disadvantage that they must of necessity be discontinuous. I bring them in at this point, inasmuch as they represent the mildest condition of the inflammatory reaction. I have not personally observed this series of changes in tissues which permit of continued study under aseptic conditions; neither am I acquainted with any observations wholly fulfilling these conditions — made, that is to say, upon transparent vascular tissues subjected to the mildest aseptic injury and examined continuously under the microscope.

The response to injury in the cases just mentioned was of the slightest. Let me now pass on to cases in which it becomes more pronounced; and in order to continue the comparative study of inflammation I would first describe the series of *events in a highly vascular and transparent region* in a low vertebrate animal, namely, in the tadpole's tail. If this be injured, either by the application of a caustic or by the introduction of a foreign inert body into its substance, a definite advance upon what was recognisable in the case of the axolotl, for example, is to be made out. Here the tail is very vascular, the wandering cells of the connective tissue are very few in number, while the blood is fairly rich in leucocytes which are small relatively to the size of the vessels. The results of injury are a congestion of the vessels, noticeable within fifteen minutes, and a well-marked determination of leucocytes to the injured region. These cells, in the main, pass out from the vessels; the few leucocytes pre-existing in the tissue appear to play a very small part. Compared with the axolotl experiment this observation is of considerable interest. Instead of a slight reaction slowly developing there is a rapid reaction; instead of a slight accumula-

tion of leucocytes there is a most pronounced accumulation. If there be any meaning in the determination of leucocytes to the region of injury, then evidently the active participation of the vessels of that region in the reactive process is fraught with benefit — it is a further important factor developed with the development and advance of the organism.

The fuller details of this vascular interference in the inflammatory process have been followed by many observers, among whom first and foremost was Cohnheim; and to this end the frog has supplied the most convenient means in regions at once vascular and fairly transparent, such as the web of the hind feet, the tongue, and the mesentery. Other observers passing higher in the scale of vertebrates have employed the mesentery of the cat, dog, and other mammalia. Suffice it to say that, with slight modifications due to local conditions in the tissue examined rather than to the animal selected, the process has been found to present the same features throughout the whole of the adult vertebrata, from the reptilia upwards. For general examination, perhaps, the best and simplest method of observing the succession of changes that follow injury of a vascular area is to be found in what I believe to be Coats' modification of Cohnheim's original experiment upon the frog's web (Coats' *Pathology*, 1889, p. 119). In order to reproduce as nearly as possible the conditions of an ordinary wound, instead of employing a caustic or chemical irritant, a small portion of the cutaneous surface is nipped off — the section being just deep enough to pass through the cutaneous layers without causing hæmorrhage. For the experiment to proceed satisfactorily, it is necessary that the frog be curarised after having been pithed. The web of a small frog is so thin that the changes occurring in and around the vessels of the part can readily be followed even with a high power of the microscope.

The first change noticeable in the immediate neighbourhood of the injured membrane is a dilation of the vessels, first of the arteries and then of the veins; and in this first phase there is a very evident acceleration of the blood flow. At this early period the capillaries show little evidence of dilation, but in the course of an hour expansion is readily distinguishable, and sundry capillary channels, previously invisible, become occupied by blood and show themselves. This first stage lasts for an hour, or in some cases perhaps two, and is followed by a phase of slowing of the blood current. While previously a well-marked axial stream of corpuscles had been evident, with a peripheral zone of plasma devoid of corpuscles, the former now broadens out, the latter becomes less and less, and as it narrows an increasing number of the clearer rounded hæmal leucocytes are to be seen in it travelling at a slower rate than the more axial stream, and every now and then stopping beside the walls of the vessels, and after a short stoppage passing on again. The leucocytes conduct themselves as if they have become "sticky."[1]

As the current becomes yet slower all distinction between axial and

[1] Even so low down in the scale as Daphnia this same peculiarity is noticeable: there in health, as Hardy has pointed out, the leucocytes move freely; but, if the slightest injury be

peripheral streams is lost; the corpuscles, closely packed together, fill the whole lumen; the leucocytes in increasing number approach the vessel walls; they adhere more firmly, and so long as a current is recognisable the action of the stream leads them to assume a pear-shaped appearance, the rounded ends pointing in the direction of the current.

As the stream slows gradually the corpuscles may move at last in a series of jerks synchronous with the heart beats; or frequently in the veins and capillaries the mass of blood may be seen moving slowly first in one direction, then in the other. Frequently one or other of these stages is followed by complete stagnation or stasis of the blood in the vessels of the injured area — I say frequently, for at other times little or no absolute arrest is seen in the vessels. Accompanying this stage, although observers employing other and chemical methods of inflicting injury have in general omitted to call attention to the fact, there is already a considerable oozing or exudation of clear fluid from the wound; there is, that is to say, an outpouring of lymph, and that apparently from the distended vessels. Now, with the slowing of the stream the leucocytes, accumulated next to the walls of the small veins and within the capillaries, pass from the interior to the exterior of these vessels; and, if the process be studied carefully with a higher power, it can be seen that this mode of passage is of an active, or apparently active nature.[1] A series of leucocytes can be distinguished some of which are rounded or flattened in immediate contact with the wall of the vein; others possess a prolongation passing into the wall; in others, again (or in the former if they be watched in the fresh specimen), the prolongation enlarges on the outer side of the small vessel while the portion of the leucocyte within the vessel becomes smaller. The final phase of this act of diapedesis is that the whole leucocyte passes through, and is found in the lymph spaces around the vessel wall. This process of diapedesis may be so general that in the course of five or six hours all the small veins of the region show a crowd of leucocytes situated along their outer surface. With these a greater or less number of red corpuscles may also make their escape.

Although the capillaries, from the very smallness of their diameters, do not show the so-called "margination" of leucocytes, nevertheless this same process of diapedesis may occur at various points along their course, so that outside the capillaries also a fair number of the same small highly-refractile cells endowed with amœboid movements can be observed.

In this modification of Cohnheim's experiment a further stage is to be recognised. While at first the fluid exuded was clear and relatively free from cells and cell débris, now, as the inflammatory process continues, an increasing number of leucocytes is contained in the exudation. The

inflicted upon the carapace, the leucocytes, previously unadhesive, soon show the tendency to adhere to the walls of the body cavity beneath the region of injury and elsewhere.

[1] The process can be fully made out if at this stage the wounded region be removed, fixed immediately in weak osmic acid, and prepared for examination by the higher powers of the microscope.

leucocytes do not remain in the immediate neighbourhood of the vessels, but many of them pass on to the injured surface; still it would seem by active amœboid movement. Thus at the end of six hours this surface may be covered by a serum or fluid in which are great numbers of these leucocytes. Here then we have the first step towards the formation of a scab or provisional protective covering to the wound.

Further observations cannot well be carried out in the pithed and curarised frog; but if an unpithed, non-curarised animal be taken, and the observations upon the earlier stage be neglected, it can be made out that if irritant matter do not find entry into the wound the process may be arrested at this point; the leucocytes upon the surface may break down, and with their breaking down and the formation of fibrin a soft scab be formed: the stasis of the blood in the distended vessels may be followed by a re-establishment of the current and slow return of the vessels to their former calibre, while beneath the thin, soft scab the epithelial cells rapidly proliferate. Within twenty-four hours there may be abundant evidence of this new growth of the epithelium tending to encroach upon and cover the wound. At the same time the region becomes less and less populated with leucocytes, so that — not to enter fully at this point into the reparative process — within sixty hours the region may show little sign of the injury and consequent inflammation.

On the other hand, if irritants of a microbic nature enter the wound the process may extend, as in inflammation of the cornea. More especially if the water in which the frog is kept become foul, there is a tendency in the inflammatory processes to spread; and in the cells of the central area, both fixed and migrated, to break down, leading to the formation of a spreading ulcer. The steps of this sequence of affairs it is difficult to follow by continuous microscopic examination, partly on account of the increased opacity of the region, partly because the process extends over days rather than hours. Here, therefore, I merely mention this possible extension of the change with its main naked-eye appearances.

It is not possible by continuous observation to make out the steps of this more extensive inflammation characterised by excessive emigration of leucocytes and destruction of these together with the fixed cells of the tissue — the pyogenetic inflammation. Several observers, however, have followed its successive stages by means of examination of affected tissues at successive intervals after the infliction of injury.

The Experimental Production of Suppurative Inflammation. — While, as shown by Councilman, Grawitz and de Barry, Straus, Leber and others, a suppurative inflammation may under certain conditions be brought about experimentally by the action of chemical irritants, such as mercury and turpentine; yet under ordinary pathogenic conditions suppuration is induced by the growth of micro-organisms within the tissues. Hence it is better to study the conditions as induced by the inoculation of pus-producing microbes into one or other tissue. A very full series of observations upon the development of abscesses through the agency of the Staphylococcus pyogenes aureus has been made by Hohn-

feldt. He employed rabbits, and inoculated small quantities of pure cultures of the microbe subcutaneously.

Four hours after inoculation the vessels of the region were found densely filled with corpuscles, and in them a commencing margination of the white corpuscles was discernible. Leucocytes were present within the tissue in numbers greater than normal; although, compared with later stages, they were infrequent. They were of two kinds—the mononuclear in the majority, the polynuclear (or more truly the form with polymerous nucleus) in lesser numbers; both forms were congregated mainly around the line of entrance of the injecting needle. Many of the connective tissue cells were so swollen as to be rounded rather than flattened. The injected cocci, lying in the lymph spaces, were scattered through the tissue; in part free, in part already ingested by cells, not only by the leucocytes, but also by connective tissue cells: the number within leucocytes was not inconsiderable.

Preparations made at the end of ten hours showed the same conditions, but more distinctly. There was ample evidence of migration of the leucocytes, margination in the congested vessels, various stages of passage through the vascular walls, and large collections of the cells in the perivascular lymph spaces; from these they spread into the spaces between the bundles of connective tissue fibrils. The cocci lay in the lymph spaces and were increased in number, and the massing of leucocytes corresponded in position to the accumulation of microbes. In these regions the leucocytes were mainly polymerous or multinuclear, but in the boundary zone away from the cocci the uninuclear form predominated.

At the end of twenty hours there was further accentuation of these conditions. As yet an abscess proper had not formed, but enormous numbers of leucocytes were present, and also of micrococci; the fibrillæ of connective tissue were widely separated by the collections of leucocytes, and these cells clustered round and hid the connective tissue cells.

With the completion of forty-eight hours a well-defined abscess had formed, separated sharply from the surrounding healthy tissue. The centre of the abscess was seen to consist of densely-packed leucocytes mingled with large growths of cocci. These leucocytes were almost entirely "multinuclear;" and in this central area the nuclei of some showed fragmentation. Neither leucocytes nor connective tissue cells showed the slightest indication of mitosis. In the central area all traces of the previous capillaries had disappeared; in the peripheral zone they were easily recognisable, being fully injected and showing a marginal disposition of their leucocytes, many of which could be seen (in osmic acid preparations) fixed in the process of diapedesis.

The majority of the cocci lay in these leucocytes. Even where the colonies of the microbes were thickest there the majority were intracellular. Passing towards the periphery the number of cocci became smaller and smaller. At the periphery they could be seen not only to be intracellular, but also free in the lymph spaces; and Hohnfeldt, with other observers, saw them definitely grouped within the endothelial cells

of the peripheral vessels. Thus it may be noted that at this stage the proliferating microbes extended into the healthy tissues outside the abscess.

In the centre of the abscess the original tissue had wholly disappeared; nearer the periphery light streaks and bundles of the disintegrating fibrillæ could be recognised between the leucocytes.

Not till about the tenth day did new growth of tissue begin to show itself. During the preceding six days there had been more breaking down of the polynuclear leucocytes, characterised by fragmentation of the nuclei and by fatty degeneration of the cell substance. But by the tenth day the periphery had begun to assume the appearance of granulation tissue; it contained numerous capillaries and new-formed connective tissue with characteristic epithelioid cells or fibroblasts possessing large oval pale staining nuclei. In these cells, as in the connective tissue cells of the surrounding healthy tissue, could the numerous steps of indirect cell division be made out. In this granulation tissue cocci were absent and leucocytes were infrequent. In the soft, cheesy central area masses of cocci were still present. Whether these were living or dead Hohnfeldt did not determine; he inferred (what has since been proved by several observers to be an unsafe inference) that inasmuch as they stained well with aniline dyes they were alive.

Thus, to sum up Hohnfeldt's observations, the processes occurring in a suppurative inflammation that ends in healing are the following: —

1. Congestion of the region of invasion, with margination of the leucocytes.

2. Collection, in the region, of uninuclear leucocytes; then diapedesis of leucocytes with polymerous nuclei: multiplication of the cocci.

3. Ingestion of large numbers of the microbes by the polymerous leucocytes and other cells, including the endothelial cells of the vessel walls.

4. Increasing immigration of leucocytes until the tissue becomes densely packed. This is accompanied by a yet greater proliferation of the microbes, which extend (*i.e.* are carried by lymph streams or by cells) into the region outside the developing abscess.

5. Destruction of the tissue of the affected part.

6. Degeneration of the leucocytes within the sharply-defined abscess.

7. Eventual proliferation of the connective tissue at the periphery of the abscess; formation of fibroblasts in the highly vascular surrounding zone; cicatrisation and encapsulation of the débris of the leucocytes and micrococci.

There are not a few points in connection with these observations of Hohnfeldt that deserve discussion; very possibly he has misinterpreted certain of the appearances seen by him. On the whole, however, he draws a full and accurate picture of the successive stages of suppurative inflammation, and I may defer discussion to a later review of the action of the leucocytes and of the formation of fibrous tissue respectively.

However, before leaving this general description of the series of

anatomical changes induced by injury, there is another phase of the inflammatory process set up by pathogenic micro-organisms which must not be passed over — I refer to those cases in which, instead of ending in repair, there is *extension and generalised disease*. The stages preceding extension vary with the nature of the microbe; thus, in some cases, the reaction to the invasion of the microbe is mainly leucocytic (as with inoculations of the micrococci of suppuration), in others it is mainly exudative or serous, the congestion of the vessels being followed by abundant exudation of serum into the tissues. This is the case in inoculation of animals — such as rabbits, guinea-pigs and fowls — with cultures of micro-organisms which are peculiarly virulent in their behaviour towards these animals. Such a serous or exudative inflammation is, for instance, well seen if the vibrio Metschnikovi be inoculated into the pectoral muscles of a fowl. Within twelve hours, it may be, the seat of inoculation becomes greatly swollen, and on section is found reddened and congested; while from it drains an abundance of relatively clear, faintly-reddish serum containing but a few leucocytes.

In such a case as this the micro-organisms appear to pass with ease from the centre of infection into the surrounding tissues, and thence into the lymphatics and general circulation, whence they may be obtained within twenty-four hours. Where there has been a well-marked abscess formation in the region of invasion there, as already indicated, it is true that the microbes may be found outside the abscess at a fairly early period; but, in the main, proliferation is limited to the abscess, and the blood remains free and sterile. Under certain conditions of great virulence of the pyogenic microbes it is found that as the abscess extends it becomes ill-defined — there is no sharp demarcation between the collected leucocytes and the surrounding tissue; the columns of leucocytes spread indefinitely from the centre, and numerous micrococci are intermingled with them. Where this is the case there is a marked tendency for the microbes to find their way into the general circulation from this irregular peripheral extension along the lymphatic spaces, and to set up a condition of septicæmia as in the more serous inflammation described above.

Septicæmia, or the passage of micro-organisms into the blood, with all the results of such a passage — the condition which sundry French observers have described as inflammation of the blood — is dealt with in another article. In septicæmia we pass beyond the local response to injury, we deal with a state of general systemic disturbance. Nevertheless certain phases of the septicæmic condition throw light upon the inflammatory process.

In the first place, it is of interest to note that when the infective micro-organisms and their products are within the vessels they fail to induce the cardinal symptoms of inflammation. They do not lead to exudation of fluid from the blood or to wide-spread diapedesis of leucocytes. The stimulus, whatever it be, which leads to these phenomena at the point of invasion is no longer called into activity when the noxa is

within the circulatory apparatus. This is the reverse of what might be expected if the inflammatory process were primarily due to a modification of the endothelium of the vessel walls by the irritant, a modification passively permitting the exudation and passage outwards of the leucocytes.

The statement that infective micro-organisms and their products circulating within the blood fail to induce inflammatory changes, would seem to need modification when the development of *metastatic abscesses* is taken into account. But a study of the mode of production of these abscesses shows that the statement still holds. Such abscesses originate round emboli of pyogenic micro-organisms in the capillaries. Sundry cocci are arrested in the capillary, proliferate and fill the vessel. It is only when a minute vessel is thus occluded that the abscess process begins, that is to say, when by this occlusion the vessel has become extravascular; and while it is true that, primarily, the arrest of pathogenic microbes within the capillaries is often associated with a small accumulation of intravascular leucocytes and with degenerative changes in the vascular endothelium, the metastatic abscess, as such, forms not by accumulation of leucocytes in the occluded vessel, but around it; the leucocytes emigrating from surrounding capillaries.

Inflammatory Fever. — In the second place, through this study of advancing inflammation it is of interest to trace the very close relationship that exists between inflammation and fever. Besides the local changes here described, local injury is accompanied by systemic disturbances. These may be slight or grave.

Take, for instance, progressive abscess formation, or follow the development of a malignant carbuncle in man. At first the reaction is purely local, but very soon, long before any of the micro-organisms are capable of detection in the blood, there is exaltation of temperature and a slight febrile state, the fever becoming more and more evident as the local process becomes more and more extensive, until with the detection of the microbe in the blood the most severe fever, with constitutional disturbance, sets in. Local inflammation, then, without any other possible explanation than either the nervous irritation to which it may give rise, or the passage into the general circulation of the soluble products of bacterial growth and tissue destruction, or both, may lead to the development of the febrile state. How large a share is played by these two possible factors it is difficult to say. That bacterial products injected into the circulation lead to the rapid production of the febrile state we have ample evidence; but whether these act directly by inducing increased cellular activity, or indirectly by stimulating the cerebral centres, we cannot absolutely say. As yet we have little accurate knowledge of the parts played by the nervous system in the development of the febrile state. This, however, may safely be declared, that the more we study the continued fevers the more do we discover that these commence by a local inflammatory disturbance. The continued fevers are the continuance, or rather the extension, of a primarily localised inflammatory lesion. [*Vide* art. on "Fever."]

Summary of the Facts thus far brought forward.

The main facts gathered thus far concerning the inflammatory process, and the conclusions to be drawn therefrom, may now be placed in order before I discuss in detail the various factors in the process. They are —

1. Injury, when it is not so widespread and severe as to lead to the death of the individual, is followed by a reaction on the part of the organism.

2. In unicellular organisms the continued vitality of the individual after injury, and in multicellular organisms the vitality of the individual cells, are dependent primarily upon the persistence of the nucleus; if this be destroyed or removed the rest of the cell is incapable of complete restitution and continued growth.

3. In unicellular organisms the reactive process is twofold, and consists of (*a*) destruction or removal of the irritant; destruction being brought about by a process of intracellular digestion, removal by extrusion of the irritant: (*b*) new growth of the organism.

4. This response to injury on the part of unicellular organisms is essentially reparative.

5. In multicellular organisms, with division of labour among the constituent cells of the individual, there is a separation of functions; the twofold reaction to local injury is yet more clearly marked; but

(*a*) The destruction or removal of the irritant is *in the main* accomplished by the wandering cells of mesoblastic origin.

(*b*) The new growth to replace the tissue destroyed by the irritant proceeds *in the main* from the fixed cells of the tissue.

6. Ascending the scale of multicellular organisms, a division of labour and differentiation of function is discoverable among the wandering mesoblastic cells. Whereas in the lower forms of the Metazoa one type of leucocyte alone is present, in the higher forms two or more varieties can be distinguished which possess different properties and act differently towards irritants introduced into the system.

7. According to the nature of the irritant causing the injury, the leucocytes are actively attracted in greater or less numbers to the region of injury, surround the irritant, and remove or destroy it by means very similar to those employed by unicellular organisms. Where the irritant is present in the form of discrete particles, there some at least of the leucocytes may incorporate the particles, and remove them or destroy them by a process of digestion. Others of the leucocytes in the higher Metazoa never act thus as phagocytes; nevertheless they are equally attracted to the focus of inflammation, and presumably tend to counteract the irritant by some other (extracellular) means.

8. While to the wandering cells appears to be allotted the main duty of removing deleterious and irritant matters, certain of the fixed cells of the organism, notably the endothelial cells of the vessels, can also exert these functions.

9. Among the very large number of Metazoan forms in which no complete vascular system is present, this attraction of the leucocytes to the region of injury is at first the sole response to injury. At a later period proliferation of the fixed cells occurs in the neighbourhood of the injury.

10. Among the higher Metazoa, in which there is a well-developed vascular system, the determination of leucocytes to the region of irritation still continues, and is in fact markedly aided by the participation of the vessels in the inflammatory process.

11. The vascular phenomena in inflammation may be regarded as serving two main purposes — (*a*) the pouring out of increased fluid into the injured area; (*b*) the afflux and diapedesis of leucocytes.

12. Even in the highest Metazoa, possessing fully-developed vascular systems, the response to injury in a non-vascular area, such as the cornea, may be associated with no change in the surrounding vascular areas, but purely with a determination to the injured area of leucocytes already free in the surrounding tissues.

13. The second phase of the inflammatory process, that of tissue repair, but very rarely occurs without evidence of previous migration of leucocytes and exudation from the congested vessels.

14. A comparative study leads inevitably to the conclusion that the determination of leucocytes to the region of injury is the most constant and most characteristic early response to injury recognisable throughout the Metazoa, and that it must be regarded as the most important factor in the first stage of the inflammatory process. The vascular phenomena noticeable in the higher Metazoa must be regarded as a second and highly important factor of later development and adjuvant. New tissue formation is the prominent characteristic of the later stages of the process.

15. As among the Protozoa, so in the Metazoa, the response to injury is consistently an attempt to repair the injury.

This general survey of the response to injury throughout the animal kingdom demonstrates most clearly that the same broad principles, the same methods of defence and repair on the part of the organism, are called into activity from the lowliest forms to the highest; that, in fact, no line can be drawn to separate one set of phenomena as truly inflammatory from another set which, while also a response to injury, are non-inflammatory. Although it is true that the term inflammation implies a reddening and congestion of the vessels, we find upon closer examination that this reddening and congestion is not the fundamental but a superadded feature in the process of repair of injury — a feature superadded as the organism advances in its place in the animal kingdom. Thus if we are to comprehend the process satisfactorily we must pass beyond the narrower acceptation of the term.

Having thus sketched broadly the general phenomena of the inflammatory process, it will be well now to describe in fuller detail the factors of this process among the higher vertebrata, and to bring together the

more important results of the study of the respective functions of the wandering cells, the vessels, the fixed cells, and the nervous system in inflammation.

PART II. — The Factors in the Inflammatory Process

Chapter 1. — The Part played by the Leucocytes

The Leucocytosis of Inflammation. — As I have already shown, there is more than one form of leucocyte in the mammalian organism, and the several forms evidently possess different attributes, and act differently in the reaction to injury. Inasmuch as these forms have been variously classified — so variously, in fact, that it is often far from easy to collate the various descriptions, and to discuss the forms distinguished by one observer in the terms of another — it is necessary to give the chief classifications of them, and their relations.

The first to discriminate between the forms of white corpuscles in the blood was Wharton Jones so long ago as 1846. He drew a distinction between

A. Granule cells { Finely granular. / Coarsely granular.
B. "Nucleated" cells — Non-granular.

His observations, together with those of Rindfleisch in 1861 and 1863, were confirmed and advanced by Max Schultze, who made out the following forms: —

1. Small round cells with round nucleus and little clear protoplasm.
2. Larger cells with round nucleus and more clear protoplasm.
3. Cells with finely granular protoplasm, and one, two, or more nuclei.
4. Cells with coarse granules in the protoplasm.

The distinctions drawn were, so far, purely morphological; and very little notice was taken of these varieties for a long period until Ehrlich, in a notable series of papers extending from 1878 to 1887, drew attention to the fact that the wandering cells of the organism react diversely towards the different aniline dyes and possess diverse tinctorial affinities indicating chemical differences in the nature of certain constituents of the cell bodies. The granules of the previous observers were found to be variously affected by the dyes employed; they were shown not to be fatty, but — as Ehrlich put it — of the nature of a glandular excretion;[1] and comparing the effects of the two groups of aniline colours — that in which the dye is associated with the acid constituent of the salt, and that wherein the dye forms the base (the "acid" and "basic"

[1] J. Weiss has studied the micro-chemical reactions of the eosinophilous granules, and concludes that they are of albuminoid nature; as they were found not to be digested in gastric juice he would ally them with the nucleins.

aniline dyes respectively) — he made out the existence of five forms of granulation associated with as many varieties of wandering cells. His table of cells according to their granulation is as follows: —

- α. Granulation — Eosinophile. — Cells frequently in horse's blood, present constantly in small numbers in human blood; numerous in medulla of bones of rabbits, dogs, guinea-pigs, etc. Stain deeply with acid aniline dyes. Granules large and coarse.
- β. Granulation — Amphophile. — Cells frequent in rabbits and guinea-pigs in blood; present also in medulla of bones. Stain both with acid and basic dyes. Granules fine.
- γ. Granulation — Basophile. — Large cells found in the connective tissue, from the frog upwards, "Mastzellen"; in blood of man only in certain cases of Leucæmia. Stain only with basic dyes. Granules coarse.
- δ. Granulation — Fine Basophile. — The "mononuclear" leucocyte of human blood. Granulation fine. Stain with basic dyes.
- ε. Granulation — Neutrophile. — The most frequent leucocyte of human blood, "polynuclear." Stain only in neutral dyes — not in acid or basic.

While Ehrlich and his pupils, and Rieder, have done much to throw light upon the relative numbers of the leucocytes possessing these different granulations in different diseases, they have accomplished little in discovering the origin of the various forms, their functions, or their relationships. We owe the first satisfactory studies upon the properties of the different forms to Metschnikoff, who, at an early period in his long-continued and wonderful series of researches upon Phagocytosis, made out that the different wandering cells of the body act differently towards microbic and other foreign particles introduced into the organisms. Thus he was led to draw a distinction between —

1. Lymphocytes — immature leucocytes.
2. Large hyaline cells, mononuclear, phagocytic, "macrophages."[1]
3. Smaller neutrophile cells, polynuclear, "microphages."
4. Eosinophile leucocytes — not phagocytic.[2]

Quite recently the admirable researches of Prof. Sherrington, and of Dr. Kanthack and Mr. Hardy, have appeared which, starting on the groundwork laid down by the older observers, have made a notable advance in the determination of the function of the various forms of wandering cells in inflammatory and other conditions. The observations

[1] While acknowledging that a certain amount of convenience attends the employment of these terms, "macrophage" and "microphage," I cannot but agree with Professor Burdon-Sanderson that they are utterly barbaric.

[2] While this article was passing through the press, M. Mesnil, a pupil of Metschnikoff, has stated that eosinophilous cells can occasionally act as phagocytes. The statement is contrary to Metschnikoff's previous observations and, I may add, contrary to general experience. Until further confirmatory observations have been made, I am not prepared to accept the statement.

of Kanthack and Hardy are especially full, and I shall have occasion to refer continually to their results. In the meantime it may be said that they materially simplify the classification given by Ehrlich, by dividing the leucocytes thus: —

1. Coarsely granular } Oxyphile cells. Staining with acid dyes.
2. Finely granular }
3. Coarsely granular } Basophile cells. Staining with basic dyes.
4. Finely granular }
5. Hyaline cells.
6. Lymphocytes.

Their coarsely granular oxyphile cells are the eosinophile cells of most writers; their finely granular are the neutrophile and amphophile of Ehrlich. They prove conclusively that Ehrlich's neutral stain is in no sense to be regarded as such, but must be considered as an acid dye.

It is now possible to collate these various classifications, and in this way to begin to study the functions of the various forms with a clear appropriation of the terms employed in the following paragraphs.

Collation of the different Classifications of the Varieties of Leucocytes.

Kanthack and Hardy.	Ehrlich.	Metschnikoff.	Max Schultze.	Wharton Jones.
Lymphocyte.	Lymphocyte.	Lymphocyte.	Small round cell I.	Non-granular nucleated cells.
Hyaline cell.		Macrophagocyte.	Large round cell II.	
Coarsely granular oxyphile.	Eosinophile cell.	Eosinophile cell.	Cells with coarsely granular protoplasm.	Granule cells, coarsely granular.
Finely granular oxyphile.	Neutrophile, Amphophile cells.	Microphagocyte.	Cells with finely granular protoplasm.	Granule cells, finely granular.
Coarsely granular basophile.	Basophile cell with γ granulation. Mastzellen.			
Finely granular basophile.	Basophile cell with δ granulation.		Cells with finely granular protoplasm.	? Granule cells, finely granular.

Lymphocyte. — Immature leucocyte; round nucleus deeply staining; scanty protoplasm; increased in number after food; diminished after starvation; indistinguishable from small elements of lymphoid tissue. Not phagocytic; variable in number; not amœboid; may form up to 30 per cent of the leucocytes present in human blood.

Hyaline Cell. — Round or kidney-shaped nucleus of slight staining power; abundant protoplasm; hyaline; non-granulated; actively amœboid and phagocytic; rare in blood (2 per cent); abundant in cœlomic fluid. Nuclei have been seen to undergo mitosis.

Coarsely Granular Oxyphile. — Large horseshoe-shaped nucleus (in man); relatively large spherules in protoplasm; highly refractive; staining deeply with acid aniline dyes; abundant in cœlomic fluid, in serous cavities, in inter-

stices of areolar tissue (K and H), and in bone marrow (Ehrlich); rare in blood (2–4 per cent); amœboid; non-phagocytic.

Finely Granular Oxyphile. — Smaller than last (in man); nucleus branching or polymerous, staining deeply; granules very small and spherical; feeble oxyphile reaction (Ehrlich's amphophile reaction in rabbit, neutrophile in man, etc.). Abundant in blood (20–70 per cent of all leucocytes); absent from cœlomic fluid; actively amœboid and phagocytic. The most common form of pus cell.

Coarsely Granular Basophile. — When found free in cœlomic fluid, round nucleus staining very feebly; spherules large and numerous, stain with basic dyes — somewhat similar cells are found stationary in connective tissue spaces — absent from human blood in health; non-phagocytic.

Finely Granular Basophile. — Spherical; smallest of the wandering cells; trilobed nucleus; clear cell substance containing great numbers of fine basophile dots. Found in human blood in small numbers (1–5 per cent); increased after meals.

From this description of the character of the various forms of leucocytes (for which I am largely indebted to Kanthack and Hardy) it will be seen that certain forms are characteristically present in the circulating blood, namely, the finely granular oxyphile and the finely granular basophile; others in the body fluid, namely, the coarsely granular oxyphile and coarsely granular basophile; while the lymphocytes and hyaline cells are common to both fluids. It must be added that the eosinophile, or coarsely granular oxyphile, are also present in small numbers in the healthy human blood: it occurs in larger numbers, however, in diseased conditions which do not come within the scope of this article.

Of the origin and relationship of these diverse cells we still know very little. As Gulland has pointed out, the blood of the embryo is entirely free from white corpuscles. The exact period at which each form makes its first appearance has not yet been studied, although in all probability such a study would throw a flood of light upon the origin of the different orders of cells.

The most that we can say with fair certainty is that the lymphocytes, while representing the larval form of leucocytes in general, are in the main derived from lymphoid tissue; that some of them develop into the hyaline cells (for, as Sherrington and others have noted, every gradation is observable between these two forms); and that what appears to be an immature eosinophile cell can often be detected in the peritoneal fluid, as also an immature coarsely granular basophile cell (Kanthack and Hardy). Beyond this we have not at present advanced.[1] Ehrlich's suggestion that the eosinophile cells are derived from the bone marrow may

[1] I quite understand that sundry observers regard all the various forms of leucocytes as modifications one of another. It is true that all embryologically have the same origin; so, for example, have the corpuscles of cartilage and bone, yet this does not make cartilage and bone one tissue. Everard, Gulland, Ruffer, Demoor and Massart, state that all transitions are observable between the various forms; I cannot but think that the methods of staining employed by these observers were insufficient for these wide conclusions. It is interesting to note that these observers, like Kanthack and Hardy, found Ehrlich's amphophile and neutrophile cells to stain with eosin, *i.e.* to be oxyphile.

be partially true, but not entirely; inasmuch as it is difficult to correlate the preponderance of these cells in the body fluid with so special and local an origin. Nor can the recent observation of Siawcillo, that eosinophile cells are abundant in the ray which possesses neither bone nor bone marrow, be regarded as favourable to Ehrlich's hypothesis. And again, the observations of Metschnikoff and his pupils render it eminently probable that some, at least, of the large hyaline cells are derived not from lymphocytes, but from proliferating endothelial cells of the lymph and blood-vessels and of serous surfaces. Finally, it is noticeable that the cells with multilobate nucleus (the finely granular oxyphile), the commonest of the hæmal leucocytes, are not to be recognised in lymphoid tissue: yet, as Sherrington has pointed out, certain of their peculiarities, notably the contorted shape of the nucleus, may be regarded as acquired, inasmuch as if they be allowed to remain at rest in the living state outside the body the nuclei become more spherical.

Of these varieties of wandering cells not all have, so far, been found to bear a part in the inflammatory process: but certain forms appear to have distinct functions therein: these are the finely granular oxyphile (neutrophile), the coarsely granular oxyphile (eosinophile), and the hyaline cells.

A word should here be said concerning the cells of later development, appearing as a result of inflammation — giant-cells, Ranvier's cells, and Gluge's corpuscles. Of these the last are evidently leucocytes of the hyaline type which have taken up the fatty products of tissue degeneration; the second — colossal cells breaking down with great ease — are of doubtful origin. Giant-cells would seem to be of more than one variety: some appear to be due to aberrant cell growth, wherein the nuclei undergo division without the protoplasm of the cell body following suit. The characteristic giant-cells of tuberculosis and chronic inflammation may now be said with fair certainty to be plasmodia, in all respects comparable to the masses of fused cells seen to form in the lower animals around foreign bodies, and by Kanthack and Hardy around masses of bacteria in the lymph of frogs outside the body. The recent observations of Borel and of Duenschmann strongly support this opinion.

Phagocytosis. — In the case of a very large number of pathogenic micro-organisms (so large a number that merely to enumerate them, with the names of the observers and of the animals upon which the observations have been conducted, makes a list so long that in the bibliographical table at the end of this article I give only the more important references, and not nearly the complete list), after inoculation into the organism, a very considerable proportion are to be discovered, sooner or later, within wandering cells which have collected in the region of inoculation. I have already mentioned more than one case of this nature in discussing the comparative pathology of inflammation. Evidently under certain conditions one of the functions of certain of the leucocytes is to attack and incorporate bacteria. The leucocytes having these properties are more especially the finely granular oxyphile (where the injection has

been into a neighbourhood richly supplied with vessels), the hyaline cells chiefly where the microbes have found an entry into the body cavity. It is, for instance, the finely granular oxyphile cell which is found in overwhelming numbers in an extending subcutaneous abscess, and these are seen to contain great numbers of the micrococci.

The conditions leading to this phagocytosis have been very fully worked out by Metschnikoff. He has amply demonstrated that the microbes can be taken up in a living condition. Thus, if the Vibrio Metschnikovi (a form closely allied to the cholera spirillum) be inoculated into the anterior chamber of the eye of an immunised animal, within a very few hours phagocytes are discovered filled with the small, slightly curved vibriones. If now one such cell be isolated, placed in a drop of

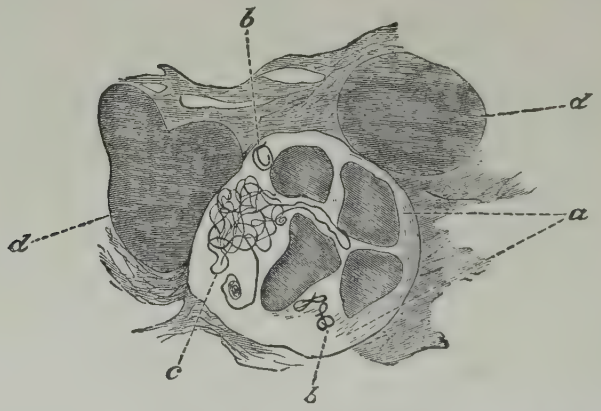

Fig. 1. — Resolution of acute infectious disease (relapsing fever), spleen pulp of monkey (Macacus erythr.), showing (*a*) microphage, multinuclear, with incepted spirochaetes; (*b*) solitary, and (*c*) forming dense tangle, (*d d*) nuclei of splenic tissue (Zeiss, $\frac{1}{18}$ ocular 4; × 1515 diam.). — [Metschnikoff (51).]

broth upon a coverslip, made into a hanging drop preparation and examined under the microscope, it is seen that the broth causes the death of the leucocyte; while with time, and favourable temperature, the microbes proliferate rapidly, and completely fill the corpuscle until it disintegrates; whereupon they proceed to multiply in the surrounding fluid. This seizing and incorporation of microbes does not then necessarily lead to their death. In certain cases of acute disease there may be abundant phagocytosis, and the disease progress nevertheless; the phagocytes being destroyed by the products of the incorporated organisms. This is the case in mouse septicæmia, in swine erysipelas, and (as has been shown quite recently by Gabritchewski) in diphtheria. As M. Roux remarks: "Ils ont fait de leur mieux en englobant les microbes, mais ceux-ci se sont adaptés au milieu intérieur des cellules, et ils ont triomphés." [1]

[1] Roux. — *Trans. Internat. Congress of Hygiene*, London, 1891, ii. p. 120.

In other less acute diseases, such as gonorrhœa; and in chronic maladies of a tubercular nature — in tuberculosis, leprosy, and glanders — the bacilli may in certain stages be found within the cells and rarely free in the lymph spaces, they appear to be almost parasitic, after the manner of the microsphæra previously referred to as infesting the amœba.

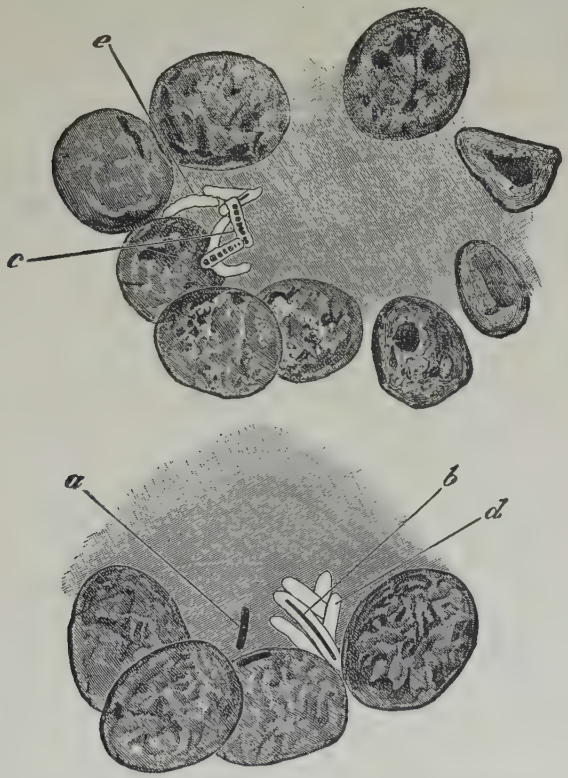

FIG. 2. — Two giant-cells, seen under high magnification (× 1515 diam.) from a rodent, the spermophile, inoculated with tuberculosis, to show stages in the destruction of the bacilli. *a*, unaltered bacillus; *b*, bacillus staining badly, and with greatly thickened capsule; *c*, bacillus granular and breaking up; *d e*, "shadows." — [Metschnikoff (51).]

In these cases it would seem as though the toxic properties of the microbes and the antagonising powers of the cells were nearly balanced. In tuberculosis, for instance, it is not unusual to find in the giant-cells some bacilli which evidently are undergoing degenerative changes, staining poorly and irregularly, or but faintly traceable as unstained, translucent shadows, while elsewhere they are apparently proliferating despite their intracellular position.[1]

[1] It is, however, unsafe to declare in all cases that because a micro-organism continues to stain well therefore it was living at the moment the preparation was taken and

And this equality, or almost equality of the resisting powers of cells and microbes, may explain the chronic nature of the diseases above mentioned. Nevertheless, in general, it may be stated that there is some relationship to be recognised between the amount of phagocytosis and the virulence of the microbe; the more virulent the microbes the less the proportion of them taken up by the cells; and, as Kanthack and Hardy have pointed out, the longer the time before the phagocytes come into action. As is the case in the unicellular organisms, so in the wandering cells of higher animals the process of destruction of the included microbes can, under suitable conditions, be seen to be digestive. Several observers have seen the anthrax bacillus, in frogs and other animals, wholly or in part surrounded by a vacuole developed within the leucocyte; and, as an evident result, the

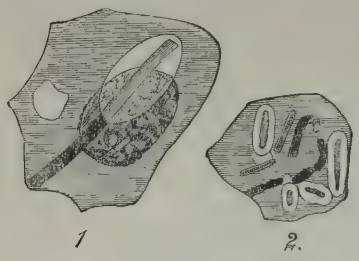

Fig. 3. — Phagocytes, macrophage and microphage, to show stages of digestion and destruction of bacilli, from spleen and eye respectively of white rat with anthrax. In *1*, part of the bacillus is unaffected, but a vacuole has formed around the other part, which further has now lost the power of taking the stain. In *2*, various stages are seen, the bacilli passing through the granular badly staining, to the vacuolated unstained, until finally but faint "shadows" are observable (Zeiss $\frac{1}{18}$, oc. 3). — [Metschnikoff (51).]

Fig. 4. — Anthrax of pigeon (an animal but slightly susceptible to the disease) to show stages of destruction of bacilli by phagocytes. *1* and *2*, macrophages: *1*, from exudation from eye of refractory bird; *2*, from muscle of region of inoculation of bird that succumbed; *3*, *4*, *5*, microphages — all from eye twenty-seven hours after inoculation; *a a*, unaltered bacilli; b^1 b^2 b^3, bacilli becoming more and more degenerated and indistinct; *c c*, débris of bacilli (Zeiss $\frac{1}{18}$, ocular 3). — [Metschnikoff (51).]

portion so surrounded has been seen to become swollen and fainter when stained, until it has undergone a veritable digestion and dissolution.

As with the lower organisms, so with the wandering cells of

fixed by heat. Thus in pneumonia after the crisis a fair number of diplococci may be found within the leucocytes of the expectorated contents of the alveoli, and these may stain perfectly well; yet it may be impossible to gain a single growth of the diplococcus from the same material.

the higher, there is an evident attraction, or chemiotaxis, whereby these cells pass towards the microbes and their products; and this chemiotaxis would also seem in general to be in the inverse ratio of the virulence of the microbes. I say in general, for with chemiotaxis as with phagocytosis there appear to be exceptions to any uniform law; and cases can be brought forward — of diphtheria, for example — in which the leucocytes, instead of being repelled, are attracted in great numbers to the region of inoculation of a most virulent bacillus.

The chemiotactic properties of the wandering cells have been especially studied by Pekelharing, Leber, Massart and Bordet, and by Gabritchewski.

Of the results obtained by these observers the most important are that leucocytes are variously attracted towards various substances. Thus Leber found that the introduction into the system of finely-powdered copper and various compounds of mercury caused an abundant collection of the wandering cells around the particles, while powdered gold, silver and iron exerted no such attraction. Gabritchewski and A. Schmidt showed that the products of bacterial growth in general possessed chemiotactic properties yet more powerful than simple chemical compounds. While the degree of positive chemiotaxis is found to vary within wide limits, the examples brought forward of negative chemiotaxis exerted by bacterial products have so far been very few — so few as to support the contention of Dr. Kanthack, that it is very doubtful whether any microbes by their products actually repel the leucocytes, though they are capable of causing the rapid destruction of the attracted leucocytes, and so of rendering the area around the microbes relatively free from wandering cells.

A very good study of the action of bacteria of different degrees of virulence can be made by repeating an experiment of Metschnikoff. The rabbit is an animal susceptible to the growth within its tissues of the bacillus of anthrax. As is well known, there are various means whereby the virulence of this microbe can be diminished; so that if cultures of the "attenuated" bacillus be inoculated into susceptible animals, these, instead of causing a fatal disease, induce but a transient local inflammatory disturbance, accompanied by fever, and followed by complete recovery. If now a small quantity of a virulent culture of the bacillus be inoculated into the one ear of a rabbit, and an equal quantity of an attenuated culture into the other, the results are very instructive. Within twenty-four hours it can be noticed that an acute inflammation has been induced in both ears; in both the vessels round the seat of inoculation are greatly congested, but whereas at the seat of inoculation of the virulent organism there is a serous inflammation so intense that the skin is raised and separated from the subjacent tissues by a clear, transparent, reddish fluid which also infiltrates the deeper tissues, in the other ear there is not nearly the same amount of swelling and serous exudation; the region of inoculation is more opaque and solid. Upon more minute examination the serous fluid in the first ear is found to

contain relatively very few leucocytes; the firmer mass in the second is composed of a huge aggregation of leucocytes [*vid.* art. "Anthrax"].

Evidently, therefore, the relative number of leucocytes migrating, and the quantity of serum exuded, depend very largely upon the intensity of the irritant; and by the intensity of the irritant, and the behaviour of the leucocytes, the forms of the inflammatory process may be classified.

But to the subject of classification I shall refer later. In the meantime it is well to sum up the theory of phagocytosis as upheld by Metschnikoff and those who see in this phenomenon the all-important factor in inflammation and the repair of injury (as also in the production of immunity), in order that, having put clearly forward the tenets of those upholding the theory, I may the more readily state wherein lies the strength and wherein the weakness of the doctrine.

The theory of phagocytosis as set forth in Metschnikoff's later writings may be summed up in the following theses: —

1. That certain of the leucocytes present in the blood and lymph, notably the finer granular oxyphile or neutrophile, and the large hyaline, are capable under certain conditions of taking up bacteria which have gained entry into the system.

2. That in addition to these the splenic corpuscles, the cells forming the endothelium of capillaries, and sundry other fixed cells of mesoblastic origin, possess the same property, although they exert it to a less extent.

3. That these phagocytes seize upon and destroy living and active microbes under certain conditions.

4. That the more virulent the microbe the less the tendency for the leucocytes above mentioned, and for the other fixed cells, to take up the bacteria. The less virulent the microbe the more extensive the phagocytosis.

5. That in addition to this power on the part of certain cells (the phagocytes) to take up and destroy certain bacteria, another factor has to be called in to explain why the wandering cells of the body migrate towards the focus or foci where the micro-organisms have gained an entry into the body. This factor is the "chemiotaxis" exerted by the products of bacterial growth, and by some other substances, such, for example, as the products of death of tissue and of wandering cells; and experimentally also certain chemical irritants as, for example, turpentine and mercury. In the case of the virulent microbes the leucocytes are not attracted to the focus of infection. There is a "negative" chemiotaxis, and thus, in the absence of phagocytosis, the proliferation of the microbes takes place without hindrance; whereas the less virulent microbes and their products attract the leucocytes, they exert a positive chemiotaxis, so that there is a migration of leucocytes through the capillary and venous walls to the focus of infection, and the leucocytes taking up the microbes tend to arrest the infective process.

6. That the leucocytes may become accustomed and eventually

attracted to substances from which at first they were repelled, and thus a negative may be transformed into a positive chemiotaxis.

7. That the cells, having once acquired positive chemiotactic properties in relation to the products of any specific microbe, retain and transmit these properties through a series of cell generations, the length of which varies according to the microbe, the extent of the primary reaction, and the idiosyncrasies of the individual.

8. That, consequently, the cure of zymotic or mycotic disease, whether localised or general, and immunity also, are mainly brought about by the activity of special cells (the phagocytes), and are primarily dependent upon the attraction existing between these cells and the products of bacterial metabolism.

9. The process of inflammation is essentially the endeavour on the part of the organism to promote the migration of leucocytes, and to aid the inclusion and destruction of the irritant. "The essential and primordial element of a typical inflammation is a reaction of phagocytes against the irritant (*agent nuisible*)." (14) Or, more fully, "inflammation is to be regarded, on the whole, as a phagocytic reaction of the organism against irritants, — a reaction which at times is accomplished by the wandering cells alone, at times with the aid of the vascular (fixed) phagocytes, or with that of the nervous system."

10. That in rare cases bacteria may be affected if not destroyed by extracellular action, by substances derived from the leucocytes and dissolved in the surrounding lymph.

In the terms of this theory, then, phagocytosis is the all-important factor in the inflammatory process, the vascular, exudative, nervous and other phenomena being auxiliary means whereby the phagocytic properties of the wandering and fixed mesodermal cells may be brought more fully into action: the determination of leucocytes that I have described is almost entirely to be attributed to an endeavour on the part of these cells to take up and destroy the irritant.

It is necessary now to ask to what extent this doctrine is to be accepted. Certainly phagocytosis is a factor in the inflammatory process — no antagonist of this doctrine nowadays is prepared to deny this — but does it occupy the all-important position arrogated to it by Metschnikoff? Metschnikoff himself admits that there are certain wandering cells — the coarsely granular oxyphiles — which never act as phagocytes. When powers so great are found to belong to one set of leucocytes, is it likely that another set, which is also especially attracted to the inflammatory focus, is absolutely devoid of either bactericidal or antitoxic function? Or, to approach the matter from another standpoint, let us take a case supplied recently by Gabritchewski from Metschnikoff's laboratory. If a guinea-pig be rendered refractory to the bacillus of diphtheria, and if the vulva be cauterised and infected by a virulent culture of this bacillus, there results a necrosis of the surface layers. On the free surface of the necrosed region lie the proliferating microbes; apposed to the under surface of the necrosed area is a large

collection of migrated leucocytes. In about three days the necrosed tissue sloughs off, and recovery and repair ensue. But in this process little phagocytosis is observable. The phagocytosis is evidently not commensurate with the extent of the inflammation; and if, as Metschnikoff urges, the leucocytes are the all-important factor, their powers of defence must here include something beyond the incorporation of the micro-organisms. The same additional something would seem to be wanted to explain the healing of abscesses.

A crucial test of the importance of phagocytosis has been devised by Baumgarten, and repeated, with like results, by Sanarelli. If microbes be placed in an animal which has normally the power of withstanding the growth of such microbes; and if, further, they be so placed (in bags of filter paper, celloidin, or pith) that the leucocytes cannot attack them, although the body fluids can easily bathe them, then, if Metschnikoff be right, the microbes ought to flourish unaffected. Baumgarten and Sanarelli found that this is not so, that the microbes are destroyed despite the absence of phagocytes; but Metschnikoff, repeating these experiments, obtained diametrically opposite results. Both Baumgarten and Sanarelli are capable observers although it is true that the former by the very violence of his attack upon Metschnikoff has materially weakened his position. It is, however, difficult to explain away their positive results, or to arrive at a conclusion other than that under certain conditions the microbes may be destroyed without being ingested.

The Humoral Theory. — The conception that there is some agency besides phagocytosis pure and simple has led bacteriologists, in the study of phenomena of inflammation and immunity, to engage in a very remarkable series of experiments. Although some of them have failed to establish a satisfactory theory of immunity, they have led to results of such high importance as the discovery of the serum treatment of diphtheria and tetanus. The majority of these researches, indeed, bear especially upon the production of immunity, and only secondarily upon the inflammatory process. It is unnecessary for me, therefore, to describe them in detail; it will suffice if I indicate the direction taken by the more important among them.

First in order of time may be mentioned Nuttall's observations. In an attempt to repeat Metschnikoff's researches upon the destruction of the anthrax bacillus, this observer noticed that if he placed a fine canula containing a fresh culture of attenuated anthrax bacilli in the tissue of a rabbit's ear, there resulted in sixteen hours a rich cellular exudation; but phagocytosis appeared not to reach its maximum for twenty-two hours, and even then half of the bacilli lay free and not taken up by cells; and he found, further, that the free bacilli showed involution and degeneration to the same extent as did the ingested. This led him to study the effect of blood serum, defibrinated blood and lymph upon the bacilli, and he discovered that these fluids had a remarkably rapid action, destroying great numbers within a very few hours. Moritz, Traube, Von Fodor and others, had previously recognised this rapid

destruction of micro-organisms in the living blood, but Nuttall's very full research appeared to show conclusively that the bacteria-destroying power resided largely in the serum, and that in inflammation the exuded fluid rather than the leucocytes brought about the destruction of the microbes.

These observations were confirmed and extended by Nissen, Behring, and Buchner, and a most valuable series of contributions (see article on the "General Pathology of Infection") have been made by Hankin, Buchner, Vaughan, Tizzoni and Cattani, Behring, and others, upon the nature and properties of the substances to be derived from the blood serum of animals either naturally immune to certain diseases, or rendered immune by one or other procedure. What is more, it has been recognised that two orders of substances are recognisable: one capable of destroying pathogenetic microbes, the other not destroying them, but rendering their products inert.

It would thus at first sight appear that in these discoveries there is a direct contradiction to the theory of phagocytosis. Yet upon further study this is found not to be the case.

As was shown by Nuttall, at the commencement of these studies, the blood serum removed from the body acts far more rapidly and energetically than do the blood plasma and lymph within the body. The disparity of action between the two is remarkable. Thus Lubarsch has shown that in order to kill a rabbit by anthrax, by injection into the circulating blood, at least 16,000 virulent bacilli of the disease must be introduced: a smaller number produces only a transient disturbance. That is to say, the whole circulating blood can only destroy less than 16,000 bacilli at a time. On the other hand, one cubic centimeter (15 minims) of rabbit's blood serum can in a few minutes kill an equal or even greater number.

The Cellulo-Humoral Theory. — If the serum and if the blood plasma contain bactericidal substances, these must in all likelihood be developed by certain cells, and thus at bottom the humoral theory must be cellular; and the very fact of the great increase in the bactericidal properties of the blood immediately on its withdrawal from the body, must suggest that in the changes which occur in the extravascular blood there is a liberation and solution of bactericidal substances. Now the first and foremost of these changes is the breaking down of the leucocytes as the blood begins to clot. It may therefore be that this breaking down of the leucocytes, with liberation of their contents, is capable of explaining the increased bactericidal action of defibrinated blood and blood serum.

That the leucocytes contain bactericidal substances was first demonstrated by Dr. Hankin, who obtained from the lymphatic glands and spleens of animals immune to anthrax (dogs and cats), a proteid of the nature of a globulin identical with Dr. Halliburton's cell globulin β, and having a bacteria-killing power similar to that possessed by blood serum. In later observations upon the rat he showed that there was a relationship

between the amount and activity of these "defensive proteids" and the power of resistance of the animal to the disease. Thus Hankin showed that in animals possessing the power of destroying bacilli, the organs containing the largest collections of leucocytes yielded notable quantities of a bacteria-destroying substance.

For the last few years I have steadily urged this view, and observation after observation is proving it to be correct. Recently Buchner has shown that if sterilised emulsions of the gluten of wheat be injected into the pleural cavity of a dog and rabbit, its presence leads to the pouring out of an aseptic exudation peculiarly rich in leucocytes, and this exudation is more bactericidal than is the blood and serum of the animal. Further, Victor C. Vaughan is led to the conclusion that the bactericidal action is associated with the leucocytes by his discovery that from blood serum a nuclein (or nucleinic acid) can be separated — a body, that is, which so far has been found exclusively in connection with nucleated cells. This nuclein is either itself bactericidal, or has a bactericidal substance in intimate association with it; and Vaughan's observations and conclusions have been substantiated by the later and independent researches of Kossel upon nucleinic acid.

Further confirmation of the correctness of these views — that the bactericidal action of the blood serum is due to the breaking down of the leucocytes — has been supplied from the laboratory of Denys at Louvain. Denys and Havel have shown that the blood and exudations of the dog, freed from leucocytes either by filtration or by centrifugal action, lose their bactericidal action, regaining it when the leucocytes are reintroduced. Van der Velde induced an exudation rich in leucocytes by injecting into the pleural cavities of rabbits sterilised cultures of the pyococci, and killing the animals at various periods. Centrifugalising the pleural fluid, he found that the older the exudation, and the richer it had been in wandering cells, the more powerful its bactericidal action, — this being out of all proportion to the bactericidal action of the blood serum removed at the same time and similarly centrifugalised.

But more convincing proof has been gained by a study of the leucocytes in action. Even in 1887 Ribbert, in his studies upon the fate of spores of various species of aspergillus and mucor inoculated into the anterior chamber of the rabbit's eye, had found that two stages of reaction were recognisable: at first the spores and developing hyphal filaments became surrounded by dense clusters of leucocytes, which remained in apposition to, but did not ingest the micro-organisms. Nevertheless they appeared to bring about a weakening and lowering of vitality on the part of the spores and filaments, so that after a time other cells could manifest their phagocytic activity and take them up. Ribbert, it is true, attributed the lowering of vitality to the walling in ("Wallbildung") by the leucocytes, and consequent lack of nutrition; but the fact remains that he demonstrated a preparatory extracellular action upon the micro-organisms by the leucocytes.

Altogether the fullest and most important studies upon this extra-

cellular action have been those of Kanthack and Hardy. In their first communication to the Royal Society these observers showed (and their experiment can be repeated without difficulty) that if a drop of frog's lymph be placed upon a coverslip, with the addition of a few anthrax bacilli, and this preparation be suspended in a moist chamber, an examination extending over four or five hours reveals the following succession of changes: —

1. The coarsely granular oxyphile cells are strongly attracted to the bacilli: they move towards them, and apply themselves to their surface; their protoplasm, ordinarily sluggish, exhibits quick streaming movements. Next the eosinophile granules are discharged, and the bacilli begin to show signs of degeneration. During this stage the hyaline cells, the phagocytes proper, remain quiescent, and are not even attracted towards the bacilli.

2. The hyaline cells proliferate and eventually approach the masses of oxyphile cells surrounding the bacilli; they fuse with these — forming a plasmodium around the chains — and for the next hour or two nothing can be clearly made out as to the action of individual cells.

3. The first stage in the dissolution of the mass is the separation and wandering away of the oxyphile cells; next, the hyaline phagocytes containing remnants of the bacilli within vacuoles slowly break apart.

4. A third set of cells, with basophile granules, is observed to approach during this last period; as to their functions Kanthack and Hardy are a little doubtful.

Here, then, we have clear evidence of division of labour among the wandering cells of the frog: the coarsely granular oxyphile cells act as unicellular glands discharging or excreting their granules, and these granules dissolving appear to exert a deleterious action upon the bacilli, in consequence of which the hyaline cells are now capable of ingesting them. I may add that occasionally the coarsely granular cells may be seen to act when not in immediate apposition to the microbes; the number of granules in a cell may diminish, and at the same time neighbouring bacilli manifest signs of partial dissolution.[1]

Continuing their research Kanthack and Hardy have demonstrated these distinctions in the function of the different forms of leucocytes throughout the vertebrata up to man. They have shown that in general the hyaline cells act as the phagocytes of the lymphatic and cœlomic system; the finely granular oxyphile (neutrophile and amphophile) as the phagocytes of the hæmal system; while the coarsely granular oxyphile (eosinophile) when present possess excretory functions.

If capillary chambers filled with bacilli or their products, or some irritant such as nitrate of silver or turpentine, were placed under the skin, or in the peritoneal cavity, and allowed to remain there for periods

[1] Mesnil, in a long and often suggestive work, which appeared while this article was in the press, contradicts these observations of Kanthack and Hardy. Apparently he never once attempted to repeat their procedure, never once attempted the simple methods necessary to confirm their results. His criticism must therefore be relatively valueless.

up to twenty-four hours, they were found to contain a multitude of cells, chiefly of the cœlomic type. If the irritant were situated in such a position as to appeal to the blood-vessels of a vascular membrane rather than to the cells of the connective tissue spaces, then the cells were those of the hæmal system. In both cases in the earliest stages there was usually found a preponderance of the coarsely granular oxyphile cells. Even in cutaneous blisters induced upon themselves, while the main mass of cells present in the serous exudation were the finely granular oxyphile of hæmal origin, the coarsely granular were always more abundant relatively to the others than in the blood. The rate of accumulation was found to vary according to the irritant. Thus, comparing the action of the virulent B. anthracis and the harmless B. ramosus upon rabbits and guinea-pigs, it was seen that if cultures of these two forms were placed within capillary tubes and introduced into the peritoneal cavity, with the former only the coarsely granular oxyphile found its way into the tubes (even after seven hours); whereas with the latter enormous numbers of the hyaline phagocytes had invaded the chambers within two and a half hours. In the former case also the total number of invading cells of all kinds was very much less than in the latter case; and there was clear evidence of the abundant disintegration and dissolution of many of the cells. This destruction of a certain number of cells occurred, whatever the nature of the microbe introduced into the system; and, as these observers point out, it must profoundly alter the chemical constitution of the plasma, and may therefore play an important part in the struggle with the bacilli. They observed phenomena of the same nature as those of the frog's lymph, when they placed anthrax bacilli in hanging drops of human blister fluid and examined the preparations upon the warm stage, noticing here also the rapid diminution of the granules of the eosinophile cells.

Finally, it must be added that Metschnikoff (while misunderstanding wholly the drift of these last-mentioned researches) has recently admitted that the wandering cells are capable of exerting an extracellular activity upon the bacteria. Certain observations of R. Pfeiffer had revealed that, under certain conditions, when guinea-pigs have been rendered highly refractory to the spirillum of cholera, these microbes when injected into the peritoneal cavity are rapidly modified, becoming swollen and spherical before any phagocytosis has time to come into play; and this alteration was explained by Pfeiffer as due to the fluid secreted by the peritoneal cells following upon the inoculation. Without detailing Metschnikoff's criticism of the value of these observations, it will suffice to say that, carefully repeating them, he discovered that five minutes after such injection the leucocytes in the peritoneal fluid — "polynuclear," mononuclear, and eosinophilous — were surrounded by a layer of spirilla, while the lymphocytes and red corpuscles were entirely free from any such surrounding. Here in the immediate neighbourhood of the wandering cells, the short, curved bacillary forms could be seen to have undergone the transformation into globules. Metschnikoff further recognised a clear

zone, evidently of exuded liquid, between the leucocytes and the spirilla. Whether this be a true secretion, or an accompaniment of the death of the cells, he is not at present prepared to say.

In this way Metschnikoff admits that, besides phagocytosis, an extracellular action of the wandering cells does occur; so that now the only point of paramount importance to be agreed upon is the extent to which the extracellular activity is manifested *intra vitam*. Metschnikoff at present holds that it plays a very secondary part compared with phagocytosis; others, like Buchner in Germany, Denys in Belgium, Kanthack and Hardy in England, hold that its part is of high importance. Personally, while holding that phagocytosis has been conclusively proved to be of singularly high importance, I cannot but see in this extracellular action of active and of disintegrating leucocytes an adjuvant to the former factor, and one which under certain conditions is even of greater value to the organism in its attempt to neutralise microbic and other irritants. Whether the fixed tissue cells of the body have similar "extracellular" action upon living irritants, or not, is a matter that has not yet been ascertained. There are indications that this may be so.

Summary. — Thus, to sum up the facts gathered together in this chapter, the chief results of recent researches into the functions of the wandering cells, as they affect our knowledge of the inflammatory process, would seem to be the following: —

1. That in the higher animals there are several forms of leucocytes.

2. That a distinction can be made out in the distribution of the various forms, some being characteristic of the blood, others of the connective tissue spaces and of the cœlom and cœlomic fluid in general.

3. That the forms of cells accumulating during the inflammatory process consequently vary according to the region of injury.

4. That a variation is to be made out also in the rate of accumulation of the different forms of cells: the coarsely granular oxyphile (eosinophilous), which in the main are pre-existent in the connective tissue spaces, being attracted sooner than the finely granular oxyphile (neutrophile hæmal) and the hyaline (cœlomic) respectively.

5. That a further distinction is to be made out in the mode of action of these cells: the coarsely granular oxyphile never act as phagocytes, but possess excretory properties; the hyaline and finely granular oxyphile are characteristically phagocytic.

6. That the accumulation of leucocytes is due in part to migration, in part to proliferation *in situ*.

7. That under certain conditions (what these are and what their relative importance have yet to be more fully worked out) the phagocytes are capable of directly incorporating pathogenetic bacteria. The main conditions would seem to be the possession by the bacteria of relatively weak irritant or pathogenetic properties, and by the organism of relatively strong powers of resistance.

8. That under other conditions (where, for example, the microbes are endowed with fuller irritant properties, or the constitutional resistance is

lower) phagocytosis may be preceded by an excretory process on the part of certain cells, notably the coarsely granular oxyphile, whereby apparently the vitality and irritant properties of the microbes undergo a diminution. Here again we are as yet ignorant of the exact value of all the factors leading to active intervention of these excretory cells.

9. That the bactericidal and antitoxic action of the blood serum and body fluids outside the body is due to the liberation into these fluids of bactericidal and antitoxic substances step by step with the disintegration of the leucocytes.

10. That clearly this liberation of bactericidal and antitoxic substances by excretion from living cells, and by disintegration, does not obtain to the same extent in the fluids within the living body; nevertheless it does occur, more especially as the result of irritation, and its occurrence is fitted to explain those cases in which the amount of phagocytosis observable is not co-extensive with the disappearance of the microbic irritants.

11. That where the bacteria are endowed with great virulence, there the wandering cells migrating to the region are both fewer in numbers, and, being killed, undergo dissolution to a very considerable extent. This dissolution may in itself, by the liberation of bactericidal substances into the inflammatory exudation, hinder the proliferation of the microbes to a greater or less extent. If, however, the dissolution be unaccompanied by a massing of active leucocytes peripherally around the region of irritation, then the microbic irritants may be carried away from the inflammatory focus, and induce generalised disease.

To complete this summary I will here add other conclusions deduced from a study of the later stages of inflammation and discussed in a later chapter ("Upon the part played by the fixed Cells in the Inflammatory Process"), viz.: —

12. In the later stages of inflammation the growing fibroblasts may often be seen to contain leucocytes in process of digestion. Presumably, therefore, a certain number subserve nutrition.

13. Others are, in certain cases, recognisable in the lymph-spaces outside the inflammatory focus, containing the debris of dead tissue. Emigration can therefore occur as well as immigration.

14. The process of development of wandering into fixed cells has been observed; but this is the exception, not the rule.

15. The contrary process of development of wandering cells from degenerating tissue (muscle fibres) has also been recorded by more than one observer.

Chapter 2. — The Inflammatory Exudation

Whenever injury to the tissues leads to vascular dilation there is an increased effusion of plasma from the blood. The extent of this effusion varies greatly; it varies with the tissue affected, the state of the organism, and the quality and nature of the irritant. Dense

tissue permits of little exudation, while loose vascular tissue, under the action of an irritant of no great intensity, may undergo great exudative swelling. There is, for instance, a peculiar liability in serous and cutaneous surfaces (or more truly in subserous and dermal layers), when inflamed, to manifest abundant exudation. Their vascularity and the slight external resistance would appear to explain this liability. There is not the same tendency to abundant exudation from mucous surfaces save where, as in the alveoli of the lungs, the epithelium is reduced to a single layer of delicate flattened cells; on the other hand there is a marked tendency towards serous infiltration and swelling of the submucosa. That some general state of the organism is a factor concerned is seen when virulent anthrax bacilli are inoculated subcutaneously into an ordinary rabbit and into one that has been rendered immune: in the former the exudation is of a serous nature, in the latter little fluid is exuded from the vessels. The effect of the quality of the irritant is observable upon comparison of the results of inoculation of various microbes. Some cause little exudation of fluid. These are in general of low pathogenic quality, but not always; certain virulent microbes (such as those of tetanus) lead, when inoculated, to relatively little effusion of fluid from the vessels. On the other hand, it may be stated definitely that where in a moderately dense tissue the injection of a pure culture of a micro-organism leads to well-marked exudation, the micro-organism is of high virulence.

Can any meaning be ascribed to this effusion? Is it an attempt at increased nutrition in the injured region? It has been suggested, in accordance with Virchow's theory of inflammation, that the injury, stimulating the surrounding fixed cells, leads to increased local metabolism; and that the exudation is a means of bringing to the region the increased nourishment demanded by the increased cellular activity. But inasmuch as exudation is most marked in those cases where there is most profound and rapid cell destruction, and again at the early stage of the inflammatory reaction, when evidences of growth and proliferation of the fixed cells of the region may be, and most often are, wholly wanting, this view can scarcely be upheld. Yet at a later period of the process, and again in chronic inflammation, the overgrowth of the connective tissue cells would appear to stand in close relationship to the over-nutrition caused by the continued dilation of the vessels and the pouring out of excessive lymph into the tissues. There is, apparently, a close relationship between the increased exudation and inflammatory hyperplasia.

That the exudation exerts a "flushing out" action is very evident in many cases. Thus the inflammation induced by plunging an animal's leg into hot water is accompanied by great increase in the amount of lymph obtainable from the efferent lymphatics of the part. It is shown also by the presence of streptococci in the lymph channels outside the area of acute inflammation in erysipelas, by the frequent implication of the nearest lymph glands in suppurative disturbances, and by the appearance

of lesions, due to the direct action of bacterial products, in organs far removed from the focus of bacterial proliferation in such diseases as diphtheria and tetanus, wherein, as a rule, the bacteria remain strictly localised. It is clear that the exudation into an inflamed area can accomplish a removal of irritant matters. It is clear also, from more than one of the examples given above, that a process which may be beneficial to the region of injury may be harmful to the system as a whole.

It is interesting to note that this effect of flushing, in part beneficial, in part harmful, has, if I may so express it, gained a certain amount of recognition on the part of the organism. Where the irritant can be conveyed to the exterior an abundant exudative inflammation generally occurs — an abundant flushing; where it can be conveyed into one of the body cavities the same holds good; but here a mechanism is often called into action whereby the exudate with its contained irritants is held within the serous cavity for days and weeks after all signs of active inflammation have subsided. The organism, that is to say, would seem to restrain its drainage to the general lymphatic system. Where the irritant is merely the product of tissue change the profuse exudate is rapidly conveyed away; where, on the other hand, the injury is of bacterial origin, the passage of lymph from the focus of inflammation, is, generally speaking, not nearly so free; it is of thicker consistency and drains away slowly. In short, as I have already indicated, where the microbe is not too virulent a cellular rather than a serous inflammation is produced; and in place of abundant flushing an increased antibacterial and antitoxic action of the exuded lymph comes into play.

But besides this "flushing out" effect the exudation subserves another purpose, namely, dilution of the irritant and reduction of its injurious properties, so that it acts with lessened force upon the tissues, and permits the wandering cells to be attracted to the region where they may exert their functions. Where a comparatively mild physical irritant leads to abundant exudation the flushing out action appears to be in the ascendant, where microbic irritants cause great local inflammatory œdema, judging from the less extensive lymph flow from the region, the diluent action must be regarded as the more important. I have already pointed out that a relation may be traced between the intensity of bacterial irritation and the extent of the exudation. In short, there may be great exudation under two apparently opposed conditions: in the presence of comparatively mild physical irritants, and in that of severe bacterial irritants. In the former case it more especially subserves removal, in the latter dilution of the poison.

The fundamental distinction between the inflammatory exudation and ordinary lymph is its richness in proteids. Whether we regard lymph as a filtrate pure and simple from the blood, or, with the majority of modern physiologists, follow Heidenhain in regarding it as the result of a selective filtration, it is eminently probable that in inflammation the exudate approaches in its composition more nearly to the blood plasma than does ordinary lymph. The dilatation of the capillaries, the conse-

quent thinning of the endothelial layer with, it may be, the opening of some lacunæ between the individual cells, and the direct action of the irritant upon these cells, may all be expected to aid the transudation. In this way the amount of proteid matter in the lymph may be increased. But equally important must be the addition of proteids due to the breaking down of leucocytes and tissue cells. I have already discussed this destruction of the cells, and need not here give the evidence of its occurrence.

In addition to the proteids the inflammatory lymph may contain other substances worthy of more than passing note. Of these the more important are ferments, the results of proteolysis (notably fibrin and its precursors, and peptones), and in many cases mucin, together with bactericidal substances, and, where bacteria are present, the products of their growth.

The presence and amount of these substances depend largely upon the intensity and character of the inflammation. Thus the total quantity of proteids, and the proportion of fibrin, albumin, and globulin present, vary within wide limits. The following table[1] of observations made by Dr. Halliburton shows well this variation in proteids, and the difference existing between inflammatory exudations and dropsical effusions: —

Pleural Fluid from	Sp. Gr.	Percentage Quantity of			
		Total Proteid.	Fibrin.	Serum-globulin.	Serum-albumin.
Acute pleurisy, Case 1	1023	5·123	0·016	3·002	2·114
,, ,, Case 2	1020	3·4371	0·0171	1·2406	1·1895
,, ,, Case 3	1020	5·2018	0·1088	1·76	3·330
Hydrothorax . . Average of three cases	1014	1·7748	0·0086	0·6137	1·1557

Between the amount of fibrin present in exudations and the amount of peptones there is an inverse ratio. Peptones are especially developed in connection with suppurative inflammation; and the more an inflammation tends to be suppurative the greater is the breaking down of the fibrin, as also of fixed and wandering cells, and the more evident the production of peptones, until in chronic abscess-formation of fair extent the peptones pass into the general circulation, and are excreted and recognisable in the urine.

Into the discussion of the mode of formation of fibrin I need not enter here, intimately connected as the subject is with the inflammatory process. The greater text-books of Physiology enter exhaustively into the matter. Suffice it to say that, as in the blood, a direct relationship

[1] These figures are thoroughly in accord with those of other analyses by Reuss, Hofmann, Mehu, and Letulle.

is made out between the breaking down of leucocytes and the development of this substance in inflammatory exudations.

It is in connection with inflammation affecting serous and epithelial surfaces[1] that fibrin is most clearly recognisable, forming, it may be, thick coatings of the badly-named "inflammatory lymph" over the inflamed surfaces. This deposit is in all respects comparable to the formation of thrombi in the blood-vessels. Here, as there, the deposit occurs only when the endothelium has undergone destruction and the roughened sub-endothelial tissues are exposed. And here also the fibrin may be deposited either in filamentous or homogeneous and hyaline form according to circumstances.

Leaving out of account coagulation-necrosis as not occurring in direct connection with exudates, it may be said that similar fibrin formation is frequently recognisable in connection with primary inflammation of parenchymatous tissues.[2]

The beneficial effects of fibrin formation in serous cavities have been rendered abundantly manifest by the increase in abdominal surgery. No one who has followed any considerable number of operations for appendicitis can have failed to remark how, in case after case, despite the intricacy of the abdominal coils and their mobility, the strongly irritant matter produced by gangrene of the appendix, or oozing through perforations in it, is restricted within a relatively small space by the surrounding fibrinous adhesions which form rapidly between the intestinal loops. By this means alone the peritonitis is restricted and "regional," instead of being generalised from the onset. Even when inflammation (as in pericarditis) affects the whole extent of a serous cavity, the layer of fibrin acts as a protective coat closing the lymphatic stomata, hindering the free absorption of the morbid material by the lymph and blood-vessels, and filtering bacteria out of such fluid as does find its way through to the tissues beneath. It is not a little remarkable to call to mind how case after case of purulent pericarditis or purulent pleurisy may be examined in which, despite the intense suppurative disturbance in the serous cavity, the tissues at the other side of the deposit of fibrin — the myocardium or the lung tissue — show little or no tendency to abscess formation. Let there be primary abscess formation or gangrene in the lung, and perforation of the pleura and hydrothorax may supervene; pleurisy, however intense, does not lead to this unless complicated by other disease. Let there be primary or metastatic abscess in the myocardium, then there may be aneurysm and rupture of the heart; yet such rupture produced by extension inwards of a purulent pericarditis is of the utmost rarity. Let there be inflammation originating in the submucosa of the intestines, as in enteric fever, and

[1] Of epithelial surfaces, more especially those covered by a single cell layer, as notably the pulmonary alveoli.

[2] Where there are abundant and distensible lymph channels there extensive clotting may be seen in the lymph. This is peculiarly well marked in the contagious pneumonia of cattle (contagious pleuro-pneumonia). In acute inflammation of various organs, by appropriate methods of staining, similar formations of threads of fibrin, often starting from cells as centres, may be observed in the tissue spaces.

perforation may result; general peritonitis, while often due to perforation, never — so far as I can call to mind — directly induces that event. In all these cases the natural protective layer of the serous surface is removed or gravely injured at a very early stage; and the layer of fibrin, replacing the serous endothelium, forms an effective barrier. I may add that the mucin, extruded so as to form a layer over inflamed mucous surfaces, presents a similar protective action.

Passing now to the ferments and ferment-like bodies present in the exudate, I may briefly state that these are not only generated and excreted by the pathogenetic bacteria present, but are liberated by the breaking down of the wandering cells. Abundant evidence of the existence of bacterial ferments capable of acting upon proteids, gelatine, sugars, etc., is supplied by the study of the growth of these microbes outside the body. That ferments also originate from the wandering cells has been demonstrated by Leber, who, placing pieces of copper in the anterior chamber of the eye, thereby produced a purulent collection devoid of microbes, and showed that the exudate was capable of digesting proteid matter.

It would seem, therefore, that, more especially in pyogenetic inflammation, the removal of dead tissue cells and dead leucocytes may, to a large extent, be due to the action of the inflammatory exudations, apart from any phagocytic action on the part of living active cells; although this also comes often into play.

Of the bactericidal substances present in the inflammatory exudate I have already treated. Here I need only repeat that the researches of Kanthack and Hardy, of Denys, and lastly of Pfeiffer and Metschnikoff, fully prove that substances capable either of destroying microbes or of hindering their growth are present therein.

Summary. — To sum up what is known concerning the inflammatory exudate, it may be said —

1. That the exudate varies in amount and in character with (*a*) the nature and intensity of the irritant, (*b*) the condition of the organism, (*c*) the region of irritation.

2. That while it undoubtedly augments the nutrition of the affected region, increased nutrition at the early stage of an acute inflammatory process would not seem to be of benefit or to play any important part. At a later stage and in chronic inflammation the increased nutrition in all probability aids the hyperplasia.

3. That in many cases the exudate exerts a beneficial action by flushing out the injured area.

4. That the exudate plays an important part in diluting the irritant.

5. That the development of fibrin in certain inflammatory exudates is associated with the breaking down of the wandering cells, and is of manifest benefit in so far as it circumscribes the inflamed area, and prevents the passage of morbid material outwards.

6. That the exudate may possess digestive functions, causing the pro-

duction of peptones; the ferments being developed from the cells alone when the exudate is aseptic, from these and the microbes together where pathogenetic microbes are present.

7. That the exudate may further contain substances, generated by the cells, capable of hindering bacterial growth, and of destroying pathogenetic microbes.

Chapter 3. — The Part played by Blood-Vessels

The study of the action and function of the leucocytes in inflammation has profoundly modified our conception of the inflammatory process. When the leucocytes were regarded as purely passive agents, and their diapedesis as purely secondary to modified conditions of the blood current and of the vascular walls, the theory of Cohnheim was that most generally accepted. And this theory regarded the changes in the vessels as of the first importance. Thus it was that for several years our attention was mainly concentrated upon the determination of the various changes of the vessel walls, and of the mechanism whereby these changes were brought about. Nowadays less attention is directed to this side of the inflammatory process, and it may be said that during the last ten years little advance has been made in determining the mechanism of the dilatation that accompanies inflammation.

The subject, indeed, is beset with difficulties. It is most difficult to observe the changes that occur in the cells forming the endothelium of the congested vessels; we are still, for instance, far from being sure whether the opinion of Arnold is correct, namely, that the leucocytes, and, it may be, a large portion of the exuded plasma, find their way out through the dilated stomata between the endothelial cells; or whether the leucocytes pass directly through these cells as one soap bubble may be passed through another. And when we come to discuss whether the inflammatory exudation be a filtration, or whether, on the other hand, it be more of the nature of an excretion, or what may be termed a selective filtration — certain components of the blood plasma being permitted to pass through, while others are withheld — we are met with the difficulty that, of the extravasated leucocytes, a varying proportion undergo rapid destruction and dissolution. Thus, in analysing the inflammatory serum, we are not dealing simply with the extravasated fluid, but with a fluid which in addition contains proteid and other constituents derived largely from broken-down white corpuscles, and in part, it may be, from the modified cells of the inflamed area.

Though Arnold's observations upon the altered condition of the vascular endothelium in inflammation appear at first very convincing, upon further study they seem at most to indicate that with dilation of the vessels there is an increase in the size of the spaces between the endothelial cells. They do not, however, prove that these are other than virtual spaces filled with intercellular substance; and indeed Arnold himself came eventually to the conclusion that some such substance was

present filling them. The fact that viscid, gelatinous substances injected into the circulation may be detected passing through these stigmata is not a proof that the spaces are actual; all it proves is that the walls are weaker in these regions: it must be remembered that increased force and increased intravascular pressure are necessary to promote the passage of the injected mass along the vessels. The passage of the mass through the walls may therefore be an "artefact."

There is this further difficulty in the assumption that these are actual spaces — that in acute inflammation the exuded fluid in general contains a smaller quantity of proteids than does the blood plasma. It is true, no doubt, that the stigmata are so small they may possibly act like the pores of a filter, and consequently may not permit the free passage of certain constituents of blood plasma. Yet, granting all this, if the same principles be in action as those governing the ordinary (non-inflammatory) transudation, we must, with Heidenhain, be inclined to regard the endothelium as playing not a passive, but an active role. To enter into the large subject of the nature of lymph would be to pass too far afield; recent researches, on the whole, favour the view that the inflammatory exudation is not a mere filtrate, but is the result of a selective activity on the part of the endothelial cells.

We have not a little evidence that these cells play an important part in the vascular phenomena of inflammation. To their power of taking up microbes and acting as phagocytes I have already referred; into their connection with the slowing of the blood stream I shall enter later. Here I would point out that microscopically these cells can be seen to alter during the inflammatory process; they become enlarged and project into the lumen of the smaller vessels, and in my experience this enlargement affects not only the cell bodies, but also the nuclei, which at the same time would seem to contain more chromatin and to stain more intensely. In cases of chronic inflammation the enlargement is followed by proliferation, notably in the arterioles and capillaries, — a process which may lead to the ultimate occlusion of these small vessels. And in acute inflammation, according to numerous observers, mitosis is to be seen occurring in these endothelial cells at an earlier period than in the surrounding tissues.

A further and very important process intimately connected with the proliferation of the endothelium of the capillaries is the formation of new vessels as the result of continued inflammation. It is true that Rindfleisch and others have described this as being brought about by vaso-formative cells situated externally to the vessels; and that others have advanced so far as to suggest that there are cells in the newly-forming granulation tissue which become hollowed out and gain attachment to the pre-existing capillaries in a manner wholly similar to that observable in the vascular zone of the chicken embryo. I have sought for such intracellular development, but never have I seen the slightest indication thereof; nor again have I been able to discover cells arranging themselves after the method described by Rindfleisch in

columns or parallel rows preparatory to the passage of blood between them and to the formation of a capillary.

The search for the earliest signs of new capillaries is a matter of peculiar difficulty. I will not peremptorily state that Rindfleisch mistook an arrangement of cells not unfrequently seen in granulation tissue for stages in the development of new vessels. I will only say that my own observations coincide with those of Arnold, and of the majority of those who have more recently studied the question, and lead me to regard the formation of new capillaries as originating from the endothelium of the vascular loops already in existence.

The first step in the process is often recognisable, in cases of pleurisy and pericarditis, in the projection of loops of pre-existing capillaries beyond the line which indicates where the serous endothelium used to be, and into the fibrinous clot now adherent to the sub-endothelial layer. Such loops are markedly distended, and "point," as it were, at right angles to the denuded surface. A similar pointing or giving way of the wall along the convex margin of the loop is also to be made out not unfrequently in newly-developed capillaries. In these there is not, as might be expected, a thinning of the endothelium along this outer margin, but certain of the cells on the contrary appear large and active. At times a small sharp protrusion of the vessel wall can be detected in the region of pointing. This is best seen in the capillaries that are themselves but newly formed, and composed of nothing but a layer of endothelial cells. In this layer the protrusion can be made out to be in direct continuity with the endothelial cells of the region. At first it is solid, but in the later stages it can be seen to be nucleated, and to be growing by proliferation of the endothelial cells which thus jut outwards. Even before any further change is noticeable in this projection from the capillary wall it may be seen to be united with a similar process originating from a neighbouring vascular loop. Finally, it would appear that the joined processes become hollowed out, and thus are developed into fully-formed capillary loops. It seems impossible to make precise observations on the phenomena of new vascular formation in its successive stages. I can but state that these appear to be the steps of the process. By what means the new vascular projections join together to form loops we are ignorant. Metschnikoff suggests that there must be an attraction between the neighbouring projections — a chemiotaxis — leading them to come into apposition; this, however, is no more than a suggestion. That they do join is very clear to those who have studied granulation tissue, or have observed the vascular network connecting the previously separated surfaces of a wound.

A further function of the vessel walls is to be seen in the slowing of the blood current. It is difficult, and in fact impossible, to explain this slowing by altered diameter of the arteries and veins. The alterations observed in the diameters of the vessels of the inflamed area are such as, acting alone, would led to increased rate of flow. Nor again is the apparent amount of exudation, and of lymph flow from the affected

part, sufficient to make it probable that (as Wharton Jones first suggested) the slowing is in the main due to the concentration of the blood, relative drying of the corpuscles, and consequent increase of friction: while this may be an adjuvant we must, I think, find some more potent factor. What this factor is was pointed out long ago by Lister, who, in 1858, noticed that coincident with the slowing of the blood stream, the corpuscles move sluggishly along the vessel wall as though attracted by it. Lister essayed to prove this by an experiment performed previously by Weber. He ligatured a frog's leg, then irritated a portion of the web by a little mustard, and found that, although the blood current had ceased, there was nevertheless an accumulation of corpuscles in the vessels of the irritated area, the corpuscles gliding into the affected region and becoming adherent there. Other observers have shown that this accumulation is not due to increased adhesiveness of the red corpuscles, inasmuch as similar slowing and stasis may be induced if the blood of the frog's leg be replaced by milk and the web irritated. In this case there is a gradual slowing of the stream of milk and accumulation of the fatty globules in the inflamed area. While in Lister's experiment the transudation of the plasma might explain the accumulation of the corpuscles, in this latter instance, as in ordinary inflammation, the observed transudation is insufficient to account for the accumulation and slowing. Although I cannot accept his experiment as conclusive, I am forced to concur with Lister to this extent, that in inflammation the endothelium of the vessel walls becomes altered, the cells becoming enlarged. With this, as evidenced by the conduct of the white corpuscles, they become more adhesive, and this adhesiveness with the associated increased friction between the vascular walls and contents I regard as the first factor in bringing about the slowing of the blood stream. Let the current once accelerated be rendered slower by this increased friction, then transudation may accentuate the accumulation of corpuscles.

Summary. — While there is very much yet to be learned concerning the part played by the blood-vessels in inflammation, and while our present knowledge of this branch of the subject can only be regarded as very imperfect, the following may, I think, safely be said to epitomise what is known at the present time: —

(1) That the vascular walls, and more especially the endothelial cells lining the capillaries, play an active and not a passive part in the inflamed area.

(2) These cells have the power of throwing out pseudopodia and of taking up non-motile bacteria.

(3) They are larger and more prominent during inflammation than they are under conditions of health.

(4) From them are developed the new vascular loops in cases of more chronic inflammation.

(5) They would seem to become more adhesive in inflammation, and by this, in the first place, to lead to the adhesion of the leucocytes and red corpuscles to their walls.

(6) Similarly they would seem to cause an increased resistance to the passage of the blood current, and in this way tend to slow the rate of blood flow.

(7) The slowing of the stream may further be aided by the passage through the walls of increased amounts of fluid from the blood.

(8) It is impossible by analysis of the inflammatory exudation to determine whether this be a mere filtrate or be the result of a selective activity of the endothelium. On the whole, taking into account the observations made upon ordinary lymph, the latter would appear the more probable.

Other properties of the blood-vessels in respect of inflammation will be better discussed in a later section in connection with the discussion of the part played by the nerves.

Chapter 4. — On the Passage of Corpuscles out of the Vessels

By his researches, Cohnheim (1867) forcibly attracted the attention of pathologists to the diapedesis of leucocytes in inflammation — a process which had already been described years before by Addison (1843) and Waller (1846) in England; and yet earlier (though without grasp of the connection between the diapedesis and inflammation) by Dutrochet, in France (1828). Cohnheim recognised the amœboid nature of the leucocytes, and saw that once outside the vessels they moved actively, but eventually he could not discover that their penetration of the vessel walls was anything but passive; and this failure on his part to recognise the true nature of diapedesis confirmed him yet more strongly in the view that the all-important factors in the inflammatory state were the changes in the vessel walls, and, it may truly be said, arrested his advance towards a fuller comprehension of the subject.

It must be acknowledged that there is much which would seem to support this view of the passivity of the leucocytes. No one is prepared to attribute active movements to the red corpuscles, nevertheless in inflammation a certain number of these escape through the vessel walls. In the inflammation affecting some organs, notably the lungs, the number effecting a passage is very considerable. If, then, the red corpuscles emerge passively, why should not the emergence of the white be passive also? Add to this the very important observations made by Cohnheim, that where the circulation is arrested by compression of the artery there diapedesis ceases. This, if invariably true, would seem to indicate that when once by changes in the vessel the leucocytes adhere to the wall, the further passage through that wall is due to the *vis a tergo* of the blood pressure.

This, however, is not a safe deduction to draw from the experiment referred to. When the artery of an inflamed area is compressed the stoppage of the blood stream not only reduces the pressure, but also affects the quality of the blood and the conditions of the vessel walls; moreover, it must profoundly affect the vitality and activity of the contained leucocytes.

These considerations alone render the experiment valueless as a proof of the passive nature of the diapedesis. Again the passage outwards of red corpuscles does not occur in the earliest stages of reaction to irritation; it never precedes the diapedesis of the leucocytes (save where there is gross injury), but follows it. A capillary or small vein in the inflamed frog's web, for example, may be seen wholly filled with corpuscles, the peripheral zone being quite annihilated, and numerous red corpuscles lying in immediate contact with the walls; nevertheless at first leucocytes only are seen to emigrate. This difference must be due to some special property of these cells. The leucocytes in the blood stream are not necessarily globular passive agents, but they are capable of independent movement. Leber, in his long series of studies, has pointed out that if, with due precautions, a hooked glass tube (closed at its outer end where it catches into the incision in the wall) be inserted into a large vein no thrombosis may be set up around the intravascular portion, and yet, upon removal, a large collection of leucocytes may be found in the tube, attracted by a drop of mercury placed within it, with normal salt solution. (Mercury is a substance which within the tissues leads to an accumulation of leucocytes.) Here, then, there must be active attraction and active movement of the leucocytes within the blood stream. And Lavdowsky has described very exactly what other observers had also noted, namely, that in inflammation the leucocytes in the outer zone of the blood stream do not simply adhere passively to the wall, but move backwards and forwards before they attach themselves and emigrate, as though seeking for a point of less resistance. At times this movement is in a direction opposite to that of the blood current.

If, then, both within and without the vessels, the leucocytes can be actively amœboid, it is strange that they should be passive in the process of diapedesis which to the eye has so characteristically amœboid an appearance.

As above stated, the compression of the artery passing to an inflamed area is in most cases sufficient to arrest diapedesis in that area, and I have suggested that this arrest may be due to the altered environment of the leucocytes. Now, if an embryonic form be taken, in which the tissues would seem to possess greater inherent vitality coupled with less sensibility, the arrest does not necessarily occur. Thus, Metschnikoff has noted that diapedesis of the leucocytes can be followed in the tadpole's tail after the animal has been curarised to such an extent that the heart has ceased to beat and the blood in the capillaries has been brought to a standstill.

It is evident, therefore, that with our present knowledge we must regard the diapedesis of the leucocytes as an active migration, and must look upon the blood pressure, the disposition of the blood stream, and the altered condition of the endothelium of the dilated vessels as adjuvants in the process. The slowing of the blood stream and the diminished pressure in the inflamed capillaries render it more easy for the leucocytes to accumulate close to the vessel wall; the dilation of the vessels and

consequent thinning of the walls, with the opening, perhaps, of larger spaces of cement substances or stigmata between the individual endothelial cells, render it more easy for the leucocytes to accomplish the passage; but the movement from within the capillaries to the tissue-spaces outside is an active process due to amœboid movement of the leucocytes themselves. The continuity of the vessel wall once destroyed, other cells — red corpuscles — may be pressed passively through the walls.

If this view be accepted, we are bound to look beyond Cohnheim's limit of changes in the vessel wall for the stimulus which, originating in the area of irritation, acts upon the vessel wall and the leucocytes in contact with it; and, having first set up changes in the former, so reacts upon the latter that they emigrate; or, to put it in other words, are attracted out of the capillaries towards the focus of irritation. It has already been shown that the movement of wandering cells in the tissue is due to the attraction of a diffusible product of bacterial growth and of tissue change, and of sundry organic and inorganic materials — a force to which the name of positive chemiotaxis has been given. This chemiotaxis must be invoked to explain the active emigration of the leucocytes from the capillaries, and again to explain its cessation under other conditions. Thus, while the exposed mesentery of a frog is a tissue in which diapedesis can be observed with facility under ordinary conditions, if it be washed with a weak solution of quinine the leucocytes in the vessels remain globular, cease to adhere to the walls, and do not emigrate. This fact, first noted by Binz, has been confirmed by several observers, among whom Disselhorst made out also that, if these same leucocytes be removed from the vessels, they exhibit their usual amœboid movements. The quinine has not paralysed them, as Binz supposed; but, as Metschnikoff pointed out, it has neutralised the previous positive attraction, a negative or repulsive chemiotaxis being brought into play. It is difficult to see how the above facts can be otherwise explained.

The view that diapedesis is an active process gains further support from, and at the same time explains certain interesting observations made by, Bouchard, Roger, and Ruffer. These observers have independently shown that in sundry instances the results of local injection of virulent cultures are greatly modified if, shortly before or coincidently, the microbes and their products are introduced into the circulation. Thus, as Ruffer points out, a drop of the culture of the bacillus pyocyaneus inoculated into the anterior chamber of the rabbit's eye leads ordinarily to a great migration of leucocytes — to an acute purulent inflammation. If, however, the toxins produced by this microbe have previously been injected into the circulating blood, no accumulation of leucocytes follows inoculation into the eye. Dr. Ruffer has also extended most suggestively certain observations of Roger. Subcutaneous or intramuscular inoculation of the rabbit with the bacillus of symptomatic anthrax leads to the production of a local abscess with extensive accumulation of leucocytes. After simultaneous injections of fluid containing virulent bacilli and their products into the vein of the ear and the muscles of the hind leg,

Ruffer found the rabbit dead, within fifteen hours, with a huge tumour in the inoculated limb. Here, upon examination, the muscle fibres were found widely separated by exudation fluid, in which there had been great multiplication of the bacilli; but leucocytes were entirely absent. In both of these cases we have therefore diapedesis and determination of leucocytes following the purely local action of the toxin; want of diapedesis and absence of leucocytes when the toxin at the same time circulates in the blood stream. If any large proportion of the leucocytes which find their way to a focus of irritation emerge from the blood stream, these divergent results are only to be explained by some theory which is capable of reconciling the difference in the action of the leucocytes when they are circulating in normal and toxin-containing blood respectively.

Now, the results in these two cases are entirely consonant with what we know concerning the sensitiveness and reaction to stimuli not only of unicellular organisms, but also of the higher animals. Organisms, whether lowly or of most complex development, only perceive and react to alteration in their environment when the alteration exceeds a definite ratio. Thus, as Pfeffer has pointed out, a motile bacterium (the "B. termo") is attracted towards solutions of peptone: if it be already in a peptone solution, in order for it to be attracted towards and move into a more concentrated solution, this last must be five times as strong as is the former. The only possible explanation that I can see of the above observations of Ruffer and Roger is that the passage and want of passage of the leucocytes out of the vessels depends upon the ratio of diffusible bacterial products present in the blood stream and in the tissues respectively. Where the products are localised at one focus in the tissues, the leucocytes are attracted out of the unaltered blood, and there is active diapedesis; where there was already a solution of the bacterial products in the blood, the ratio of difference between the percentage amount of toxin in blood and tissue may be insufficient to stimulate the leucocytes; no diapedesis then ensues.

As is well shown in the experiment with symptomatic anthrax, the presence of the bacillus and its products in the circulating blood did not prevent inflammation at the region of local injection; inflammation and exudation were abundantly manifest — there was, in fact, a more extensive exudation than ever. The irritant — that is to say, the toxic products of the bacilli — at the point of injection was in no wise hindered from exerting effects upon the fixed cells of the vessel walls, and promoting all the changes in calibre and condition of the walls and in the blood stream characteristic of inflammation. But with vascular changes, if anything more prominent than in the case where local inoculation alone had been practised, the leucocytes stayed within the vessels: now the only cause to which we can attribute this abstention of the cells from emigration, is lack of attraction — certainly not lack of vascular change or lack of blood pressure.

Summary. — I am thus led to the following conclusions regarding

the passage of cells out of the blood stream into an inflamed area: —

1. The diapedesis of the leucocytes is, as the name implies, an active and not a passive process; it is due to active amœboid movements on the part of the cells.

2. The stimulus leading to diapedesis is that of positive chemiotaxis. It is the attraction exerted upon the leucocytes by the diffusible substances associated with the irritant.

3. Irritants, if themselves diffusible, or the diffusive substances developed while the irritants are within the tissues, are capable of two separate actions: one direct upon the vessel walls, leading to vascular changes; the other through the walls upon the leucocytes, whereby emigration may be induced.

4. These two actions need not (and frequently do not) manifest themselves pari passu.

5. In relation to diapedesis, the dilation of the vessels, the altered rate of blood stream, the altered disposal of the corpuscles in the stream, and the modified endothelium, may all be regarded as adjuvants.

6. The passage of red blood corpuscles from the blood-vessels into the inflamed area is passive, due to the blood pressure and to lack of continuity of the vessel walls. Such lack of continuity is afforded in many instances by the migration of the leucocytes through the walls.

Chapter 5. — On the Part played by the Nervous System

If the vascular changes in inflammation were due to reflex influences proceeding from the central nervous system, and were in fact controlled by the centres in the brain and spinal cord (as has been held by the supporters of neuro-humoral theories) then, in the first place, there should be a rapid and almost immediate response on the part of the vessels of any region on the introduction of an irritant. But this is not by any means constantly to be observed. Thus, as Cohnheim pointed out, if croton oil be rubbed upon a rabbit's ear more than an hour may elapse before the first beginnings of hyperæmia can be detected; yet the inflammation eventually set up may be very intense. In the second place, section of all the nerves passing to any region of the body should have this effect, that injury in the region in question should be unaccompanied by the ordinary vascular reaction. But this is not the case. Divide all the nerves which supply a rabbit's ear for example, and then injure that ear, either by heat, cold, or inoculation of pathogenetic micro-organisms, and inflammation manifests itself with all the stages recognisable in an ear with intact nerve-supply. The vascular changes which accompany inflammation can occur then independently of any central nervous influences.

We can proceed farther, and state that regions deprived of their nerve-supply are peculiarly prone to inflammatory changes. But this liability to inflammatory disturbances in such regions is not directly due

to the destruction of vaso-motor tracts and the cutting off of central influences from the vessels of the part, but is, it would seem, immediately connected with the loss of sensation. Divide the ocular branch of the fifth nerve of a rabbit, and, if the eye be not protected, ulceration and necrosis of the cornea manifest themselves in the course of a few days. Protect the eye, either by bringing the lids together or by placing a shade over it in such a way that dust and foreign particles are prevented from settling upon the surface, and no such ulcerative disturbance manifests itself. From this it is clear that the primary cause of the inflammation is not any trophic change in the region, but is the lack of sensation, whereby irritant substances are permitted to gain a lodgment upon the outer surface without any attempt being made to remove them. That, in addition, there is a lowered vitality in parts deprived of their nerve-supply, and that this renders those parts a more favourable seat for inflammatory disturbances is more than probable; nevertheless, this would not seem to be the primary cause of the increased liability to inflammation. [*Vide* art. on "Nutritional Retrogressive Changes."]

This, then, in the first place, is clearly recognisable—that the vascular changes accompanying inflammation can occur independently of central nervous influences. Hence it follows that there must be a peripheral nervous mechanism controlling the vessels. It remains, therefore, to determine the nature of this peripheral mechanism: is it wholly under the guidance of peripheral nerve cells situated in the vessel walls, or is it, in part at least, idiopathic? In the present state of our knowledge the answer to this question must be guarded. The more carefully the innervation of the various regions is studied, the more clearly is it demonstrated that throughout all the tissues of the body there exists a wonderfully fine and complicated network of nerve filaments with occasional isolated ganglion cells. Yet proof is wanting that this system in connection with the vessels is sensorimotor. Indeed, so far as regards the heart and ventricular muscle (which may be looked upon as the region of the vascular system wherein the motile portion of the walls has become specially developed), the researches of Romberg and His lead rather to the conclusion that the peripheral nervous system subserves sensation alone.

Dr. H. J. Berkley's careful series of researches recently brought together in a *Johns Hopkins Hospital Report* (Neurology II., 1894) throws much light upon the termination of the nerves in various organs, and upon the relation of these nerves to the vessel walls. Berkley finds in connection with the ventricular muscles a dense network of nerve filaments, with small bulbous terminations upon the individual fibres. These observations, it must be admitted, tend to weaken the belief in the idiomuscular, or, more truly, idioneural action of the heart muscle.

At the same time, the more the activity of the various tissues is studied, the more fully it is seen that many cells retain what may be termed reminiscences of an earlier and more embryonic condition in which their functions were varied and less specialised. There is an

inherent probability that the endothelial cells can react directly to stimuli, and that they are capable of idiopathic contraction and expansion on appropriate stimuli. We have seen that these cells are capable of taking up microbes, and thus seem to exhibit an independent activity similar to that observed in the amœba or the wandering phagocyte. If these cells, then, are capable of throwing out pseudopodia, and thus of enclosing non-motile bacteria, are they not capable of contracting and expanding, as a whole, according to the stimulus of altered environment? As a matter of fact, such contractility of the endothelial walls of the capillaries has been demonstrated by Klebs and Severini. I cannot but conclude, then, that the endothelium of the capillaries is to some extent self-regulative or neuro-muscular. It is quite possible — but "non-proven" — that the muscular coats of the smaller arteries are likewise capable of self-regulation, and respond directly to stimuli.

This view — that the vascular phenomena of inflammation can occur independently of the central nervous system and of the peripheral nerves — does not imply that the nervous system, central and peripheral, is without its influence upon the process; far from it. We have evidence, in the first place, that the state of the vascular walls is modified after destruction or severance of the nerves. I do not here refer only to the consequent alterations in calibre of the vessels, but also to the changes in other properties. Thus Gergens, and to a less extent Rütimeyer, noticed that after destruction of the spinal cord the blood-vessels of the frog permit a larger quantity of fluid, and even particles of granular colouring matter, to permeate them.

In the second place, we have evidence that the central nervous system exercises some direct influence upon the inflammatory process. From Cohnheim onwards it has been a matter of common observation that when all the nerves of a part have been severed, the stages of the process succeed each other with greater rapidity. It may be that the modified state of the capillary walls, noted in the preceding paragraph, is capable of accounting for this fact, and that, in the absence of central influences, dilation of the vessels and exudation of fluid lead to the cardinal symptoms of redness and swelling, with associated changes in the tissue, at an earlier period.

Of the part played by the different sets of nerves the external ear of the rabbit again furnishes an excellent study. This part has a double nerve-supply through the auriculars (major and minor) passing from the cervical plexus and the sympathetic branches proceeding from the superior cervical ganglion: stimulation of the former leads to dilation of the ear vessels, of the latter to contraction of the same. If, as shown by Samuel, the sympathetics be divided on the one side, and the auricular branches upon the other, the ear vessels of the former side become widely dilated, and those of the latter markedly constricted. Under these conditions, if both ears be subjected to the action of water warmed to 54° C., there is a characteristic difference in their reaction. In the organ deprived of sympathetic influence the

congestion and hyperæmia become yet more pronounced: an acute inflammation sets in which proceeds rapidly to recovery. In the opposite ear, with its constricted vessels, no hyperæmia is set up; but there is stasis, and gangrene may supervene. These results have been confirmed by Roger, who, taking a rabbit and dividing the sympathetic on one side and then inoculating both ears with like quantities of a culture of the streptococcus of erysipelas, found that the erysipelatous process manifested itself much more promptly upon the paralysed side, and came to an end at an earlier date. The reverse was the case when the auriculars of the one side had been divided: here the process was of slower development than on the intact side, and of slower course, resulting in mutilation of the organ.[1]

The inference to be drawn from these observations is that section of all the nerves passing to the rabbit's ear permits the inflammatory process to run a more rapid course; section of the sympathetics (vaso-constrictors) alone has the same effect; while the uncontrolled action of the sympathetics after section of the auriculars (vaso-dilators) hinders or prevents the manifestation of the ordinary processes of inflammation, and by preventing the destruction or removal of irritant matter favours necrosis of the tissues. We have yet to learn whether these results are capable of a general application, and to discover how far they are borne out by clinical observations on diverse cases of localised paralysis. So far as they go they afford direct evidence of the power of the central nervous system to modify the course of the inflammatory process, while they demonstrate admirably how potent an auxiliary is the dilation of the vessels in the inflammatory process.

Other evidence that the state of the nerve-supply of a region influences the manifestation of inflammation is afforded in sundry neuropathies. In all of these, in the present state of our knowledge, it is difficult to trace out the nervous factors associated with the lesions to which I refer. Our knowledge of the respective influences of trophic and vaso-motor nerves is far too limited to permit us to say more than that a relation exists between the condition of the nerve-supply of the affected area and the inflammatory lesions there observable; that in a certain number of cases inflammation affecting the area supplied by one branch of a nerve may have associated with it definite inflammatory disturbances in the areas supplied by other branches of the same nerve, and that, similarly, when inflammation affects a viscus, inflammatory phenomena may be sympathetically developed in regions innervated from the same area in the brain or spinal cord. I have already given examples in support of the first statement: the familiar redness, swelling, heat and pain of the side of the face which may accompany toothache is an example in support of the second, while the condition of labial herpes in pneumonia is an evidence of the results of

[1] Although these results have been criticised by Samuel and other observers, upon reviewing carefully the whole literature of the subject, I cannot but think that the above paragraph represents the general trend of more recent work.

the third. Another example is to be found in the acute nephritis, which at times rapidly follows the passage of a catheter, or the impaction of a stone in the urethra. It is not unlikely that many of these sympathetic inflammations are not direct, but secondary. Thus, the first noticeable symptom of catheter fever is suppression of the urine. Such suppression might be brought about either by reflex contraction of the renal arteries, or, contrariwise, by reflex great dilatation and congestion of the vessels of the kidneys. If it be caused by the former then the nephritis can only be regarded as secondary, and as due to the injury done to the organ by the stoppage of its blood-supply for some little time.

From the multitude of the factors involved, these examples, taken separately, afford at most only a great probability that the nervous system can directly originate inflammatory changes. There is, however, the clearest proof that the nervous system does possess this power, and this is afforded by the results of certain observations upon hypnotic effects. There are persons susceptible to hypnotic suggestion, in whom the suggestion that a red-hot substance has been placed upon the hand will, in the course of a few minutes, lead to great reddening of the part supposed to have been burned, and this reddening may be followed by great local exudation and swelling — in fact, by all the symptoms of acute inflammation. Here then actual inflammatory reaction follows supposed injury.

It is unnecessary to do more than point out the light that this intervention of the central nervous system throws upon the subject of counter-irritation, and upon the modifications of the course of inflammations brought about by idiosyncracy of the individual.

From what has been said in the preceding paragraphs, it follows that: —

1. Acute inflammation in all its stages may proceed regularly in the absence of all centrifugal nervous influences.

2. The vessels of an injured area are capable of reacting apart from central influences; it may be either directly, or under the control of a peripheral system of nerve cells.

3. The central nervous system is capable of modifying the process of inflammation. It would appear that when the vaso-dilators alone are called into action the successive stages of the process are accelerated. When the vaso-constrictors alone are acting the process is retarded.

4. Centrifugal impulses alone, apart from any local injury, may originate a succession of phenomena of inflammation in a part.

5. Hence, in all probability a nervous and central origin must be ascribed to some, at least, of the sympathetic inflammations seen to occur in areas supplied by the other branches of a nerve supplying a part primarily inflamed; and again in areas supplied from the same region of the brain or cord as the inflamed organ.

Chapter 6. — On the Part played by the Cells of the Tissues

As a consequence of irritation two opposed processes may be manifested in the cells of the affected area, — changes leading to impairment and death, and changes leading to overgrowth and proliferation; degeneration and regeneration.

Either of these two processes may, it is true, be wholly wanting. In very acute suppurative disturbances, destruction of the tissue cells and the steps leading to destruction may be the only recognisable changes. Again, in the first stage of most injuries, whether of mechanical, chemical or bacterial nature, degenerative changes are wont to take the lead. On the other hand, there are irritants so mild that little or no cell destruction results from their action; an extreme example of this category of inflammations is seen in those epithelial overgrowths commonly known as "corns," due, as Sir James Paget pointed out in his lectures, to intermittent pressure and irritation of moderate intensity.[1] Other examples are to be found in the "catarrhal" inflammations, in which there is marked initial overgrowth and proliferation of the cells of mucous membrane; and in tuberculosis, again, in which characteristically the earliest effects upon the pre-existing cells, produced by the presence and growth of the tubercle bacilli, are those of enlargement and multiplication — necrotic changes, as a rule, only appearing at a much later stage. Once more, in the later healing stages of injuries, cell proliferation may be in the field alone. Nevertheless, in a very great number, if not in the majority of inflammations, the two processes may be found occurring together — destruction and degeneration being in evidence at the focus of irritation, and growth and proliferation towards the boundary zone, where the irritant is acting in a less concentrated form.

Although the two processes are thus so frequently associated, it will be well, for the orderly review of our subject, to consider them separately.

Degeneration of the Tissue Cells. — Death of the pre-existing cells as an immediate consequence of injury cannot be regarded as one of the phenomena of the inflammatory process. Immediate death of the cells may be a result of injury, and the disintegration of the dead cells may in itself lead the way to all the symptoms of inflammation. But cessation

[1] It may very well be that this is not an extreme example. Neoplasms as a class, whether malignant or benign, not improbably develop as a consequence of some irritation having an intensity just sufficient to induce cell proliferation, and continued for a time sufficiently long to impress upon the cells of the affected tissues the habit of rapid multiplication. There is evidence both in animal and vegetable pathology favouring this relationship between inflammation and neoplastic growth.

The objection may be raised, with considerable force, that substances which lead to cell-proliferation are stimuli and not irritants, and that a line should be drawn between inflammation proper and overgrowth the result of irritation. I, for one, would willingly make this difference, but while it is easy to draw the line in certain well-marked examples, in others, as I shall proceed to show, cellular proliferation is so essential a part of the whole inflammatory process that the division becomes impossible.

of action is not reaction, nor is failure response, and throughout this article inflammation has been considered as the reaction following injury, and the response to it. Thus immediate death of tissue cells is resultant and not reactive, and may be eliminated from the category of the essential phenomena of inflammation.

The same is to some extent true of cell degeneration, but not entirely. While it is impossible nowadays to accept Virchow's old view, that inflammation is essentially a process characterised by increased nutritive changes in the cells of the tissues, it remains most probable that in very many cases irritation induces increased, even if perverted, activity of certain orders of cells. The proliferation, swelling, and more or less rapid degeneration of these cells cannot be wholly ascribed to the toxic influence of the irritant, but must in part be regarded as a result of over-stimulation and overwork. This is most noticeable in connection with catarrhal and parenchymatous inflammations. In parenchymatous nephritis, for example, such as that set up by cantharidin or septic infection, the cells especially affected are those whose functions are especially excretory; and their degeneration would appear to be intimately related to the performance of their functions. Such degeneration, preceded or accompanied, as it so frequently is, by excessive proliferation, may truly be regarded as reactive, and not as wholly and primarily destructive.

Of the degenerations which affect the tissue cells in inflammation (and often at the same time the leucocytes) there are many varieties; in fact, according to the nature of the irritant, one, or other, or all the degenerations affecting the tissues in different pathological conditions may manifest themselves, save, perhaps, simple atrophy and pigmental degeneration (as apart from pigmental infiltration). Most commonly recognised are cloudy and fatty changes, but mucoid and hydropic changes are far more frequent than is generally noted. Even so specialised a change as amyloid degeneration has been observed occurring locally in chronic inflammations — as, for example, in gummata; while in these same chronic lesions hyaline degeneration in the vessel walls is very often to be encountered.

There is also to be seen in inflammatory disturbances of moderately acute type a further form of degeneration, which receives a passing mention in the text-books, it is true, but so far has not to my knowledge been duly treated as an entity; nor has its significance been fully grasped. This is what may be termed "reversionary" degeneration. It is to be seen affecting tissues, in which the individual components in the fully-formed state are not single cells, but cell complexes or compounds. Such compounds are the voluntary muscle and medullated nerve fibres, and, as Grawitz has pointed out, the fat cells of connective tissue.[1] These are formed by the fusion and united growth of several cells;

[1] I here, and throughout this article, leave wholly out of account Grawitz's "slumbering cell" theory — a theory incapable of actual proof, and at variance with the cell theory upon which is based the entire superstructure of modern biology.

and in inflammation, as under other pathological conditions, the degeneration of the cell-compound as a whole manifests itself by a certain amount of proliferation of the nuclei (of the muscle fibre, sheaths of Schwann, and periphery of the fat cells respectively), protoplasm can be observed to accumulate around these active nuclei, and with the assumption by the component cells of an independent existence the degeneration may be said to be complete — that is to say, beyond this point only the shell and débris of the original compound are left to be considered.

All these degenerations are inevitably associated with disturbance of the functions of the affected cells, and lead to their death if the irritation which has induced them be continued. But death is not the final stage to be considered. The ultimate fate of the necrosed cells varies according to the situation of the inflamed area, the intensity of the irritation, and the specific character of the irritant. From a free surface the dead material may be freely cast off. In acute suppurative inflammations, whether superficial or deep, and, in general, wherever there is an abundant determination of leucocytes, there obtains a digestion and solution of the necrosed cells; and, as I have already pointed out, this is associated with the development of peptones and albumoses, and is brought about largely through the extracellular action of the leucocytes. When there is a large area of cell destruction, with well-developed encystment and limitation of necrosis by granulation tissue, there the solution of the dead material and subsequent absorption may be incomplete, and a fatty débris left behind, which may eventually become infiltrated with lime salts (the calcareous degeneration falsely so-called). In tuberculosis, despite the presence of many leucocytes in the immediate vicinity, the dead material of the centre of the tubercle undergoes very little absorption, but remains as an inspissated, cheesy mass. In syphilis, on the other hand, in large gummata, while there is similar death of the central cells and absence of removal, fatty metamorphosis does not occur nearly to the same extent.

Lastly, although very little is known about the subject, attention must be drawn to the fact that along with the tissue cells the intercellular matrix undergoes modifications or degenerative changes during inflammation. Among these, in all probability, is to be classed an increase in the amount of intercellular mucin, a mucoid degeneration. The inflammatory exudate is in many cases rich in mucin, and although our knowledge of the changes in the matrix is scanty, the fact that the tissue cells in general show little evidence of storage of mucoid or mucinogenous material, renders it probable that what mucin is formed is either excreted or elaborated between the cells. Connective tissue fibrils, which may be regarded as part of the matrix, undergo dissociation and swelling, and eventually, in acute inflammation, disappear. In chronic disturbances they are especially prone to hyaline change.

Regeneration of the Tissue Cells; Overgrowth and Proliferation. — In the lower animals, as we know, injury and actual removal even of a large portion of the body may be followed by the complete reproduction of

the lost part. In man, however, this reproduction of lost tissue is reduced to its lowest point; the higher the tissue the less, and the less perfect, the reproduction. Speaking generally, the tissues which show the greatest potentiality for reproduction are the least highly organised — those composed of similar units. The "connective tissue" — the lowest and most widely distributed — retains the largest powers of proliferation and hyperplasia.

In ordinary inflammation hypertrophy and hyperplasia of the connective tissue cells are absent at the focus of irritation. Here degeneration is predominant. It is in the peripheral zone, away from the maximum concentration of the irritant, that (as shown in case after case of Leber's long series of studies upon injury to the cornea), the connective tissue cells show signs of enlargement and proliferation, that they become more swollen and prominent, send out large processes, and may exhibit signs of active mitosis. It may be urged that this peripheral change is not inflammatory, but associated; yet, as I have already hinted, the signs of cellular regeneration may manifest themselves at so early a stage that it is impossible to disconnect them from the process of inflammation. This fact has been brought out with emphasis in Ranvier's interesting series of studies on irritation of the peritoneum by weak solutions of caustic substances. If a few drops of a 0·3 per cent solution of silver nitrate be injected into the abdominal cavity of a rabbit or guinea-pig an inflammation is set up which lasts for some days. At the end of twenty-four hours the portions of the serous coat of the abdominal contents which have been most affected are found denuded of their endothelium — the cells have died and disappeared; but in other regions, less strongly affected, the endothelial cells present the reverse condition of overgrowth: their nuclei are swollen; the protoplasm, instead of forming a flattened plate, is swollen, and presents stellate prolongations anastomosing with those of neighbouring cells. The underlying vessels at this period show abundant evidence of inflammation; they are congested, and leucocytes are being poured out into the mesenteric network. Within forty-eight hours there follows upon the inflammatory exudation a rich development of fine filaments of fibrin, and along sundry of these filaments the enlarged endothelial cells send processes. Some of the cells become enormous, 100 μ or more in diameter. In this extension of the cells along the fibrinous framework we have probably the commencing formation of organised adhesions. The endothelial cells at this stage have become so modified from their previous quiescent flattened state that even outside the body they exhibit amœboid movements.

Up to this time no signs of nuclear division manifest themselves. According to Toupet, working under Cornil, it is not until the fourth day that mitosis is recognisable in this form of inflammation. But while inflammatory congestion, exudation of fluid, and diapedesis of leucocytes is proceeding actively, the modified endothelial cells of the regions that have not undergone the severest injury are with equal activity engaged in what it is difficult to regard as other than a reparatory process.

As Baumgarten showed in his studies upon the development of tubercles, in the irritation set up by the growth of the B. tuberculosis in the tissue, a like overgrowth with proliferation of the fixed cells occurs in the immediate neighbourhood of the bacilli without any primary evidence of cell degeneration. It is true that of late the researches of Borel have thrown doubt upon Baumgarten's observations, but they confirm the earlier researches so far as regards the mitosis of pre-existing cells, and the absence of degeneration of these in the earlier stages of the tubercular growth. Borel would regard all the large epithelioid cells of the tubercle as modified leucocytes. For myself I cannot admit that he has proved this, careful as his researches seem to be; and until the leucocytic nature of these cells be firmly established I am inclined, with the majority of histologists, to regard many of them as similar in nature and origin to the modified cells just described in connection with simple inflammation.

The difficulty of determining the origin of the growing cells in inflammation has formed the greatest trial of the pathologist throughout an entire generation, and yet longer; nor can we now assert without chance of dispute what cells are mainly concerned in the formation of new tissue.

When we examine newly-formed granulation tissue we can distinguish cells of more than one type — (1) small round cells with polylobular and fragmented nuclei, (2) other cells containing oxyphil granules, (3) larger cells with a single nucleus and a relatively large quantity of protoplasm, and again (4) cells of varying but generally large size, varying in shape, but on the whole having the appearance of spindle cells with single oval nucleus and abundant protoplasm. These can be made out easily.

The first two forms of cells are clearly leucocytes. Further study of their fate shows that they disappear; they play no further part in the organisation of the tissue save that, as is well shown by Scheltema and Nikiforoff, many of them are absorbed by the growing connective tissue cells, and thus would seem to aid in their nutrition. The last form likewise presents, as such, no difficulties. These are fibroblasts — cells in the process of growth into connective tissue. But what is their relationship to the previous form, — to the round mononucleated cells with fairly abundant protoplasm, — what are these last, and what in short is the origin of the fibroblasts, — is it from leucocytes or from pre-existing connective tissue cells? Upon this most difficult question more ingenuity and more research have been expended than upon any other part of this well-worked field of inflammation.

There can be no doubt nowadays that a large proportion of the fibroblasts in granulation tissue are developed from pre-existing connective tissue cells. The general consensus of recent researches leads decidedly in this direction; and it is from the laboratory of Ziegler, who by his classical observations led pathologists for some years to hold the contrary view, that the studies have emanated which most conclusively show the part played by the connective tissue; the researches of Krafft,

Podwyssozki, Cœn, Fischer, and Nikiforoff, confirmed and strengthened by the researches of Arnold, Marchand, Reinke, and Sherrington, all bring forward evidence in one direction. It is the clearly recognisable pre-existing cells of the tissue — connective, endothelial and epithelial — which show most constantly the signs of nuclear division: every stage of enlargement, mitosis and cell division, can be made out in them. Even if we did not possess the information afforded by nuclear changes, the fact that new tissue is always developed in the immediate neighbourhood of pre-existing tissue would in itself point strongly to this same conclusion.

We may rest assured of this much. But can we advance farther, and state that all newly-formed connective tissue cells originate from the pre-existing cells of the tissue, and that none of them are derived from wandering cells? In the present state of our knowledge the answer to this question must be an unhesitating "No." If we base our observations upon the morphology of the cells in granulation tissue, we find that with our present methods the large, round, mononuclear cells seen therein are undistinguishable on the one hand from large hyaline leucocytes, on the other from one stage in the development of fibroblasts. If we examine into their properties we find that they act as phagocytes incorporating the multinuclear leucocytes. The fibroblasts, according to Nikiforoff's careful studies, have an identical action; so also, according to Metschnikoff, Ruffer, Borel, and others, have the large mononuclear hyaline leucocytes. If we study their mode of division they, like the connective tissue cells, exhibit indirect or nuclear division. It may be (as has been more than once suggested) that the large mononuclear hyaline leucocytes differ from the other forms in being of endothelial origin. Were this so a path would be found out of our present difficulty. Certainly the most that can now be said is that it is quite possible that among the higher animals this one form of wandering cell may be contributory to new fibrous tissue formation, quite possible that the connective tissue cells which develop as a result of inflammation are not all derived from the pre-existing cells of the region.[1]

It must be borne in mind that leucocytes, endothelial, and connective tissue cells are very simple forms of tissue, that they are all of like mesoblastic origin, and thus being homogeneous, may be more variously modified, without impairment of activity, than more highly specialised cells. I must here add that in lower forms — in the tadpole's tail, for example — Metschnikoff has followed day by day the transition from leucocyte into typical connective tissue cell, and that, largely in consequence of these observations, French pathologists hold the view that the leucocytes enter far more actively into new tissue formation than I here recognise. The German school, with the exception of Arnold (whose

[1] In this connection may be mentioned the observations of Metschnikoff, confirmed by Barfurth, and more recently by Dr. Joseph Griffiths, which show that in the degeneration and disintegration of muscle fibres (of the tadpole's tail) the proliferated nuclei of the fibres become the nuclei of individual wandering cells — leucocytes.

views correspond on the whole with my own), has with Ziegler passed over to the opposite camp of connective tissue only from connective tissue. For myself I have carefully sifted the evidence adduced by either side. What is said above gives, I believe, the estimate of the matter for the time being; while what follows gives in brief the state of our knowledge of the part played in inflammation by the tissue cells in general.

(1) Two series of changes may occur in the cells of an inflamed tissue, which may be included under the terms degeneration and regeneration respectively.

(2) The extent to which one or other of these series of changes predominates varies with the nature and intensity of the irritant.

(3) Degeneration and death of the tissue cells may be a direct and immediate result of the presence of the irritant, and then can scarcely be regarded as essential phenomena of inflammation. Or they may be of more gradual onset, associated with evidence of over-stimulation and increased activity of the cells.

(4) Fatty, cloudy, hydropic and mucoid are the most frequent forms of degeneration affecting the tissue cells in acute inflammation; hyaline in chronic; other forms are rare.

(5) The ultimate fate of the necrosed cells varies as the situation, intensity of irritant, and specific character of irritant.

(6) Cell-proliferation is so constant an accompaniment of certain forms of inflammation that it is impossible to regard this as an adjunct and not as an essential part of the process.

(7) The tissues which show the greatest potentiality for reproduction in consequence of inflammation are those which are least highly organised.

(8) The origin of fibroblasts and new connective tissue cells cannot be regarded as entirely determined, but this much would seem to be clearly demonstrated: (α) That a large proportion of the fibroblasts are derived from pre-existing connective tissue cells. (β) That in lower forms — as, for example, the tadpole — leucocytes can be seen to develop into connective tissue cells. (γ) It is quite possible, indeed probable, that in the higher animals one form of wandering cell, the large hyaline mononuclear, contributes to the formation of new fibrous tissue.

Chapter 7. — On Fibrous Hyperplasia and its Relationship to Inflammation

The succession of changes from embryonic cells to fully-formed tissue can best be studied in cases where there has been a relatively large area of destruction — as, for example, after severe burns, or excision of organs or large portions of organs; or again, where inflammation has been of a chronic character.

If healthy granulation tissue be examined, the process of growth is seen to originate in the immediate neighbourhood of if not in direct

connection with the dilated new capillaries. It is around these vessels, formed of little more than a single layer of cells, that the fusiform fibroblasts are in greatest abundance. At a later stage, in regions more remote from the advancing margin of the granulations, the fibroblasts have a more general distribution in the intercapillary spaces, and are more elongated; around them may be seen the earliest wavy fibres of white connective tissue. These are essentially of cellular origin — as much so as is the substance of striated muscle fibres. The elongated fibroblasts not only break or extend at their poles into fine processes, but also along their sides the protoplasm undergoes modification into fine parallel fibrillæ. With the continuance of this change the cells become smaller and smaller until little is left but the attenuated nuclei, often so flattened and narrow as to be scarcely recognisable. It is generally accepted that the fibrillar substance contracts with increasing age; certainly the newly-formed cicatricial tissue diminishes greatly in volume, and with this diminution the previous great vascularity of the part disappears; the capillaries shrink until the majority become completely occluded. Thus in place of the abundant, soft and succulent granulation tissue, rich in cells, blood-vessels and exuded fluid, there is eventually a firm, shrunken, anæmic mass of fibrous tissue, with rare flattened nuclei, rich only in closely-pressed bundles of white, semi-transparent fibrils.

Fibrous hyperplasia is to be encountered in almost every tissue of the body as a sequence of very diverse morbid conditions. To speak of it in any case as "fibroid degeneration" is a misnomer. The overgrowth of any tissue, however lowly, is not a degeneration. Fibrous tissue may and often does become the seat of degenerative processes, notably the hyaline; but that is another matter. To regard every condition of generalised or localised fibroid change of the organs of the body as a chronic "—itis" is equally erroneous, until we have proof absolute that connective tissue only undergoes excessive growth directly or indirectly under the stimulus of injury. It is interesting to note the opposed tendencies of the two branches of our profession on this subject; the surgeons strive to restrict the idea of inflammation to acute pyogenic disturbance, the physicians to extend the idea so as to include all cases of chronic progressive "fibrosis." I will not say that the latter is as untenable a position as the former, for it is a matter of peculiar difficulty and delicacy to state what is and what is not an inflammatory fibrosis; after all, there is more danger of being tossed about helplessly in the Charybdis of including too little, than there is of striking upon the Scylla of including too much in our idea of inflammation.

Here I wish to point out how divergent are the conditions which lead to fibroid hyperplasia, and to draw attention to the fact that there is reasonable ground for not classing all forms under the one common heading, even though the resulting appearances may be undistinguishable and the effects the same.

Cicatricial fibrosis presents little difficulty; it is plainly the result of

inflammation; so too is the fibrous overgrowth upon chronically inflamed serous surfaces. Capsular fibrosis is clearly of the same nature; it is to be seen around foreign bodies, around chronic abscesses, in the walls of tubercular cavities, and encapsulating tubercles, gummata, and other neoplasms inflammatory and non-inflammatory. Allied to these is the fibroid replacement in old infarcts (including that following upon "myomalacia" cordis). Here, studying a series of cases, it can be made out that the necrosed material becomes surrounded by a zone of inflammation, and that, with the passage of leucocytes into the dead area and absorption of the effete material, there is soon manifest a new connective tissue overgrowth advancing inwards from the periphery.

Among the generalised scleroses there is one form frequently encountered which may, without hesitation, be regarded as the accompaniment of inflammation. This is seen well in the general interstitial nephritis accompanying subacute and chronic parenchymatous inflammation of the kidney. Of similar nature are some forms at least of hepatic cirrhosis, diffuse syphilitic cirrhosis, the diffuse tubercular cirrhosis to which attention has more especially been drawn by French pathologists, and an extensive pericellular cirrhosis in cattle, which I have of late been engaged in studying, due, it would seem, to the abundant multiplication of a diplobacillus in the bile capillaries and liver substance. Whatever be the immediate cause of other forms of cirrhosis, overgrowths of fibrous tissue would appear in these to precede atrophy of the liver cells, and to be associated with the presence of an irritant.

But there are other varieties of fibroid growth concerning which it is less easy to arrive at a just conclusion. First may be mentioned the replacement or compensatory fibroses. An excellent example of this is to be seen in the sclerosis of well-defined tracts of the spinal cord following destruction of the ganglion cells governing those tracts, or sections of the fibres, at a point proximal to their trophic cells.

The fibrosis in these cases is not secondary to a progressive inflammation, but to a simple atrophy of the nerve fibres. These shrink, and their place is taken by fibrous tissue. Another equally instructive example is to be found in the dystrophic sclerosis of the cardiac muscle fibres to which attention has been called, more especially by Drs. Martin and Huchard. This occurs in certain cases of arteriosclerosis, and is best seen in the papillary muscles, the fibroid change occurring, not around the thickened arterioles, but at the periphery of the area supplied by each. The muscle fibres around the arterioles are healthy; but farther away, through lack of nutrition, they have atrophied, and their place is taken by a zone of fibrous tissue which frequently manifests hyaline degeneration. In this instance the morbid condition of the arteries is in itself a hindrance to active dilatation of the vessels, and the exhibition of the ordinary accompaniments of inflammation. Indeed this peripheral zone is singularly free from leucocytes, yet well-marked sclerosis appears nevertheless.

Can these be regarded as cases of inflammatory fibrous hyperplasia? According to our definition they may: the fibrosis ensues as a reaction to injury. It is legitimate to conceive that the dying and atrophic tissue elements here, as in the grosser condition of infarct, act as irritants. But, on the other hand, the only recognisable evidence of inflammation is this very extension of cicatricial tissue; and even this is strictly limited in amount, being just sufficient to replace the dead tissue, and nothing more.

Active hyperæmia is not a prominent characteristic of any stage in the first instance cited above, and is throughout absent in the second. Still, as I showed in an earlier portion of this article when treating of injuries to non-vascular areas, active hyperæmia is not absolutely indispensable.

Active hyperæmia is entirely wanting in yet another form of fibrosis — that resulting from passive congestion, whether of the blood (as in clubbed fingers, in that variety of cirrhosis of the liver which may result from obstructive lung or heart disease, and in the spleen of portal obstruction), or of the lymph (as in chronic œdema, sclerema, elephantiasis and macroglossia). Is this to be regarded as an inflammatory fibrosis? Everything points to the conclusion that connective tissue cells and their progenitors, like the Chinaman and the Polish Jew, can thrive and multiply upon a pabulum which is starvation to those of a higher standard. In passive congestion, as in obstruction to the onward flow of lymph, there results undoubtedly a bathing of the tissues with increased lymph. Can this alone account for the hyperplasia, or must we invoke the aid of the irritation or stimulus of retained effete matters contained in the lymph? This question is one that is most difficult to answer. Underlying it are the further questions whether one broad explanation can be found to apply to all cases of tissue hyperplasia; and whether cell growth in general, under physiological as under pathological conditions, is due to increased nutrition, or to stimulation of the cells, to increased physiological activity of the same, or to removal of pressure and other conditions preventing growth, or to a combination of all, or nearly all of these. This last question at present remains unanswered. In the examples before us of hyperplasia following passive congestion, one possible factor, that of removal of pressure from the cells, is absent; and we are narrowed down, I think, to two of the possible factors named above — relatively increased nutrition, and stimulation by effete matters. If it were shown that there are states in which stimulation or irritation by effete matters plays no part in the overgrowth of new connective tissue, then we could, I think, safely declare that forms of fibrous hyperplasia exist which cannot come under the heading of inflammatory fibrosis, and that the fibrosis of passive congestion may be included among them.

Now such conditions do exist. That increased nutrition alone can lead to hypertrophy of the tissues was established long ago by Hunter's classical experiment of transplanting the cock's spur on to the cock's comb, —

moving it from a slightly vascular to a richly vascular region. In the ensuing overgrowth there can here be no question of irritation by anything beyond the normal blood.[1] And passing from the general to the particular, we have evidence that there is such a condition as fibrous hyperplasia due, as it would seem, to increased nutrition unassociated with the presence of toxins or other cellular irritants. In his wonderfully painstaking series of observations upon arterial changes, Thomas has adduced two cases which he describes, no doubt, as examples of endarteritis, but in which the inflammation is not apparent, nor indeed any factor other than altered tension of the arterial walls leading to altered conditions of nutrition. He shows that immediately after birth there is developed a thickening of the intima — a connective tissue proliferation immediately below the endothelium — of that portion of the aorta lying between the ductus Botalli and the passing off of the umbilical arteries. During later fœtal life the umbilical arteries are the largest branches of the aorta; and, when the circulation through them is arrested, the aorta above is too large for the amount of blood requisite for the abdominal viscera and the lower extremities. The arterial current becomes therefore relatively slowed, and presumably, judging by the analogy of what occurs in the adult when large branches of the aorta are ligatured, the aortic blood pressure is for a time raised. With this slowing and increased pressure there appears a compensatory overgrowth of the intima leading to contraction of the vessel and its lumen. Generally speaking, when the area of distribution of an artery is diminished, as, for example, when a limb is amputated, the artery shows a similar proliferation of the intima. In both cases the blood remains healthy, and the intima has undergone no injury; the only recognisable change has been a slowing of the blood stream, and probably increased blood pressure; and as the intima is nourished, not through the vasa vasorum, but directly from the main arterial fluid, it would appear that with the slowing an increased nutrition is brought into action. I can see no satisfactory reason for calling either of these cases an endarteritis. It is quite possible that other cases of thickening of the intima are due not to irritation, but to increased nutrition brought about by heightened arterial tension. The difficulty urged by Councilman that high arterial pressure does not invariably lead to overgrowth of the intima is not, in my opinion, insuperable. It must suffice if here I point out that it is more than probable that certain cases of endarteritis are in no sense of inflammatory origin, or secondary to degenerative changes; but are primarily associated with nutritional changes. In this connection it was shown by Prof. Roy and myself that when the aorta of the dog is suddenly and greatly constricted, and as a consequence the pressure in the

[1] I here leave out of account a factor which may be important, but about which we know practically nothing — namely, the effect of altered innervation. I am forced to assume, perhaps wrongfully, that, as this factor plays a like part in all the cases under consideration, it may for present purposes be disregarded.

proximal portion of the vessel greatly increased, the plasma of the blood is forced into the cusps of the aortic valves, and vesicles of lymph make their appearance on the under surface in that region where fibroid thickening is most frequent in cases of chronic high arterial pressure.

Thus, to express briefly the distinction that I would draw between inflammatory and non-inflammatory fibrous hyperplasia, I would say that where *local injury* leads to increased nutrition of the connective tissue, with increased functional activity of the cells, the ensuing fibrous hyperplasia is to be regarded as of inflammatory origin; where, on the other hand, local injury is not recognisable as the primary cause of the cell growth, the hyperplasia must be held to be non-inflammatory. In passive congestion, obstructed lymph-flow, and increased nutrition consequent upon arterial change, as in the cases cited above, we can so far see no cause for the fibrous hyperplasia beyond altered conditions of nutrition; there has been no primary lesion in the affected regions inducing the reaction. Such cases must be considered as non-inflammatory.

But while I lay down this distinction, I must impress upon the reader that the last word has by no means been said upon this matter, and that further research may cause a radical reconstruction of our opinions.

Forms of Fibrous Hyperplasia

A. *Of Inflammatory Origin.*

Localised
1. Cicatricial.
2. Perivisceral.
3. Capsular.
4. Replacement—
   Gross (of infarcts, etc.).
   Fine (dystrophic sclerosis, etc.).

Generalised
5. Cirrhotic, associated with parenchymatous inflammation, interstitial and lymphangitic.

B. *Of Non-Inflammatory Origin.*

1. Hyperplasia of increased (arterial) nutrition.
2. " of venous congestion.
3. " of lymphatic obstruction.

C. *Neoplastic.*

1. Fibromata.

Upon the Increased Temperature of Inflamed Areas

Very little has of late been added to our knowledge in this division of our subject: what is to be said appears now to be so well established that I need do little more than state the main conclusions. The long controversy that raged before these conclusions were fully accepted, and

John Hunter's original views shown to be in the main correct, scarcely comes within the scope of this article.

1. The temperature of superficial regions is raised, it may be several degrees above the normal, by the onset of inflammatory hyperæmia.

2. The temperature of internal organs when inflamed may be raised above the normal, but undergoes no material increase beyond that of other unaffected internal organs tested at the same time.

3. The rise above the normal, which is often present, is an indication of the febrile state accompanying the inflammation, and not of locally increased heat production.

4. The increased temperature of superficial areas when inflamed is due, not to the production of heat in the part, but to the increased quantity of blood passing through it. When the congestion is so great that stasis ensues there may be actual decrease in the temperature of the part.

5. The maintenance of high external temperature may exert a favourable effect upon the duration and progress of specific inflammation. Thus Filehne has recently shown that the course of experimental erysipelas in rabbits is more rapid and more benign when they are kept at a high temperature than at a low. We possess no clear evidence that this is due to the unfavourable effect of the heightened temperature on the growth of the microbes. Pasteur's well-known experiments upon the production of anthrax in fowls (ordinarily insusceptible to this disease) by lowering their temperature can be explained on other grounds. We have abundant evidence that heightened temperature promotes vascular dilation: the experiment of Filehne may therefore supply a further demonstration of the favourable effects of dilation of the vessels and hyperæmia in the inflammatory process.

6. Low external temperature, or the application of cold to the surface, contracts the vessels: hence, upon the lines of what has already been said, it would appear that

(*a*) It is calculated to diminish the amount of exudation.

(*b*) It is calculated in consequence to diminish the pain associated with inflammation.

(*c*) It has no directly good effect upon inflammation due to the presence and growth of pathogenetic micro-organisms, but may have the reverse effect of preventing the fullest reaction on the part of the organism.

(*d*) Where the irritant does not itself grow and multiply, or present cumulative action, there the application of cold may not only be of no harm, but of positive advantage, by lessening the inflammatory reaction and preventing this, where extensive, from being itself a cause of further injury to surrounding tissues.

The increase of systemic heat will be considered in the article on Fever.

PART III. — On the Various Forms of Inflammation

Chapter 1. — Classification

The minute changes which characterise the process as it affects one or other organ, and the various specific forms of inflammation, will be fully described in special articles. I have only to indicate more general causes and main varieties. To give a complete classification is impossible unless each separate tissue be taken in order, for each tissue presents peculiarities either in liability to inflammation, or in the course assumed by the process. Even to attempt a classification in broad outline is beset with difficulties, for the inflammatory manifestation varies, not according to one or two series of causes, but according to four at least; the permutations are thus so numerous, and the appearances so varied, that to give an adequate scheme of classification would require a diagram in four dimensions. These four causes of variation are —

A. Nature of tissue affected. B. Position of tissue affected. C. Intensity of irritation, or more correctly ratio between resistant powers of the organism and intensity of the irritant. D. Nature of irritant.

A. Nature of Tissue affected. — As I have already shown in the first portion of this article, there is in the earlier stages of the process a difference in the reaction of vascular and non-vascular tissues, the one series exhibiting marked congestion and vascular disturbance, the other not. At a later stage, or in more chronic irritation, as new vessels invade the non-vascular areas, the changes in the two series do no doubt approximate; but in the earlier stages we may distinguish between an ordinary inflammation and "inflammatio sine inflammatione."

The relative denseness and compactness of the tissues also introduce characteristic alterations: a dense tissue, such as bone, does not show the signs of reaction to injury to nearly the same extent as does a loose tissue — such as the omentum, for example — thus, in the former there may be a process almost as atypical as in non-vascular areas. The rigid framework of a tissue like bone prevents great vascular dilatation and exudation, but at the same time may be the seat of great pain due to pressure of the confined exudate upon the nerve endings. The loose connective tissue of a structure like the omentum, on the other hand, permits great exudation with little or no pain.

The influence of structure is well seen in comparing the course of inflammation affecting cutaneous, mucous and serous surfaces respectively. Where we have to deal with cutaneous surfaces, or surfaces formed of squamous epithelium, there the increased exudation, and the resistance offered by the layers of flattened cells to the free exit of the exuded fluid, lead towards the formation of vesicles or blisters. In the case of serous surfaces, which form the walls of a moist cavity, the irritant, affecting primarily but one portion of the surface, is very likely to be borne into the cavity with the exudate and to set up an inflammation

extending over a very large portion of the surface. Mucous and cutaneous surfaces, which are not thus the boundaries of cavities, exhibit a more marked disposition to the production of localised inflammation and of ulcers; the superficial layers indeed of a well-formed epithelium or mucous membrane, by the protective powers of their cells, form a defence against irritation from without: thus the superficial exudate from a region of local inflammation cannot easily produce a superficial extension of the process.

Not only the nature of the tissues, but their function also, profoundly affect the character of the inflammatory manifestation. Thus, excretory organs, by the very nature of their function, during the attempt to remove noxious substances from the system, are especially liable to generalised parenchymatous inflammations, — the irritation not being local, but affecting at the same time all the cells whose part it is to take up and excrete the irritant bodies.

B. The Position of Tissues. — It is difficult to consider the position and relationship of tissues as they affect the inflammatory manifestations, without continually touching upon their structure. Nevertheless, the two, though very closely connected, do not go hand in hand.

A familiar instance of modification in form brought about by position is to be seen in the result of suppurative inflammation — in the development of ulcerous conditions when the process affects free surfaces, of abscesses when it attacks deeper tissues. The process in the two cases is virtually the same: there is the same abundant determination of leucocytes, the same degeneration of them into pus. Yet apart from the gross difference in form, there are minor differences between the two. There is, for instance, relatively much more serous exudation from the free surface of an ulcer than there is into and around an abscess. As a general rule, inflamed tissues near a free surface are the seat of more abundant exudation. Of this liability for free surfaces to be the seat of serous inflammation I have already spoken. The skin, with its thick dermal layer, affords a good example: when the full suppurative stage is not reached, inflammation affecting the outermost layers of the derma is most often of a vesicular or œdematous character; when it affects the deeper layers of the derma the serous infiltration is less evident.

Yet another example of the influence of position in modifying form is seen in enteric fever. In this malady, the lymphoid tissue forming the Peyer's patches becomes the seat of excessive cellular infiltration and proliferation, undergoes necrosis, and is cast off, leaving the well-known ulcers. The lymphoid tissue of the neighbouring mesenteric gland likewise undergoes great infiltration and enlargement, but necrosis rarely implicates the whole of a gland: notwithstanding the previous extensive inflammation, the glands commonly recover their normal appearance and size.

Beyond this there are few broad principles to be laid down concerning the relationship between forms of inflammation and position that do not essentially depend upon the structure and functions of the tissues.

Much can be said concerning the intimate connection between position and liability to inflammation; but this and the allied and most important subject of the protective mechanisms of sundry tissues against injury are away from our present point.

C. The Relative Intensity of the Irritant is a more frequent and potent cause of variation. I have already in several places referred to the ratio between the resistant powers of cells and the intensity or virulence of the irritant as it affects the inflammatory process, and have shown how much that was previously vague has been made clear by bacteriological research; while, at the same time, it has brought home the truth that the various forms of inflammation merge insensibly one into the other.

Broadly speaking, it may be stated, as a result of these studies, that, *cæteris paribus*, increased virulence of any given microbe or diminished power of resistance on the part of the organism or of the tissues, leads to corresponding alterations in the phenomena of inflammation at the region of inoculation; and *vice versa*.

Thus, if a pathogenetic microbe, such as that of anthrax or erysipelas, be greatly attenuated, the effects of inoculation into the subcutaneous tissues may be scarcely recognisable. If the attenuation be not so extreme some hyperæmia, a determination of leucocytes, and, relatively, very little exudation, will be seen; and in the course of a day or two all traces of inflammation may have disappeared. With slightly more virulent microbes the migration of leucocytes may be followed by their breaking down and consequent abscess formation; with further increase of intensity of action the migration of leucocytes may be wanting, while the exudation extends and the inflammation rapidly spreads and leads to a septicæmia. A like series of changes is observable if the strength of virus be constant and animals more and more susceptible (or less and less refractory) be inoculated.

The variation in tubercular lesions, from isolated dense fibroid masses to loosely formed cell accumulations and diffuse tubercular inflammation, is evidently explicable on this law. The law holds good also, not merely for bacterial products, but for other irritants also. The effect of croton oil varies with the strength of the solution applied; and, as shown by Samuel, according to the condition of the animal. The same is true of abrin and other vegetable extracts.

Turning to physical irritants, while here the intensity of the irritant alone or almost alone is called into play, numerous examples can be given of the effects of variation in this one respect upon the inflammatory manifestation — effects of cold, for instance, varying from chilblain through inflammatory œdema to gangrene; of heat varying from hyperæmia through vesicular inflammation to complete destruction of tissue; and, again, effects of caustic substances. In this era of aseptic surgery we may forget what was well known to the last generation of surgeons, that caustic substances may be employed either to originate a benign and reparative inflammation (as in the case of indolent ulcers);

or, in larger quantities or greater intensity, to bring about a state in which the death of the tissue elements is far in excess of the subsequent repair. Thus then, according to the above-mentioned ratio, inflammation in a tissue may vary by insensible gradations from a mere hyperæmia up to a spreading suppurative or gangrenous process; and from a purely local manifestation to the development of what may be termed an inflammation of the whole organism.

D. The Nature of the Irritant. — It is clear, then, that it is impossible to base a classification upon the nature of the irritant: the attempt to mark off sharply the inflammations caused by mechanical and chemical noxæ from those produced by bacteria and their products must be given up. Hüter's proposition that suppuration can only be induced by microbes has been repeatedly shown to be erroneous. Thanks more especially to the researches of Councilman, Leber, Grawitz and de Bary and Straus (many more names might be mentioned in this connection), we now know that many chemical substances are capable of causing pus formation.[1] Among these may be mentioned turpentine, croton oil, mercury, copper and silver nitrate. On the other hand, although this pyogenetic property is not confined to microbes and their products, yet among microbes it is not the common property of all. Some, like the bacillus of tetanus, never in themselves induce pus formation: others, like the bacillus of tuberculosis, lead characteristically to tissue growth and the formation of inflammatory neoplasms rather than to pus formation. Even among those which, like the micrococci, are highly pyogenetic, the formation of abscesses only occurs when there is a definite relationship between the virulence of the microbe and the resistance of the organism. The reverse is equally true, that numerous microbes, not specially pyogenetic, produce pus under peculiar conditions. Thus, the bacillus of enteric fever, when it multiplies in the middle ear, induces a suppurative otitis, and, as Dr. C. F. Martin has shown, it is further capable of originating a suppurative arthritis.

In fact, under varying conditions the same microbe can induce very various forms of inflammation. Thus, Charrin has shown that the B. pyocyaneus and its products are capable of inducing in one organ — the kidney — pathological conditions so diverse as acute, chronic, parenchymatous, interstitial and thrombotic nephritis, with, in addition, cyst formation and amyloid degeneration.[2] This same microbe can induce acute suppuration in the anterior chamber of the eye; and when inoculated into the blood cause a hæmorrhagic inflammation of the serous surfaces. Hence we can proceed further and state that no strict classification of inflammation can be made according to the nature of the

[1] While this is so, it must be borne in mind that under ordinary conditions these substances very rarely act upon the organism in a state of sufficient concentration to be pyogenic. Thus, while it is impossible to make a sharp line of demarcation between bacterial and chemical irritants, it holds true in the main for man that suppurative disease is an indication of the presence and growth of microbes.

[2] These changes are comparable with the diverse conditions of the kidney in the human being brought about by the scarlatinal virus.

bacterial irritants: it is, however, possible to make a general grouping of those affecting man, as follows: —

(i.) Micro-organisms characteristically leading to pus and abscess formation — Staphylococci and streptococcus pyogenes, B. anthracis.

(ii.) Those leading to abundant exudation with necrosis — B. of malignant œdema.

(iii.) Those leading to cellular infiltration without usually causing abscess formation — B. typhi abdominalis, M. gonorrhœæ, B. diphtheriæ, etc.

(iv.) Those inducing characteristically the development of inflammatory neoplasms — B. tuberculosis, B. pseudo-tuberculosis, B. mallei, Actinomyces, Aspergillus fumigatus.

Similarly, chemical substances may roughly be grouped into —

(*a*) Substances causing so slight an irritation when introduced into the organism as to induce cellular overgrowth only in their immediate neighbourhood — such as bland foreign bodies, bullets, etc.; inhaled particles of coal, stone, iron, and the like, conveyed into the pulmonary lymphatics.

(*b*) Substances leading to vesicular inflammation, *e.g.* blistering agents, such as cantharides. (This result, however, depends more upon the position than the nature of irritant.)

(*c*) Substances leading to cell necrosis, followed by the formation of granulation tissue — caustic agents.

(*d*) Substances leading to cell necrosis and suppuration, such as copper, mercury, mineral acids, etc. (a very rare result in man).

These lists, from the considerations given above, are necessarily unsatisfactory and imperfect.

Other Considerations. — Among other factors varying the inflammatory process may be mentioned the duration of the action of the irritant, which of necessity must modify the extent of the manifestations of disturbance in the tissues. A simple aseptic incision, for example, leads to a much milder and slighter series of changes than do the prolonged presence and growth of the tubercle bacillus. Yet while at first it might appear an easy matter to name case after case where the irritant has but a momentary action, upon further consideration it is found that, in the majority of cases of purely mechanical injury, this is not the case; or, to express the matter more exactly, in the case of physical injuries, it is not the act of wounding that causes the inflammation, but the damage inflicted upon the cells of the tissues; as, to a very large extent, inflammation is set up by the products of the injured and destroyed cells. A bone may be suddenly broken, and nevertheless, even under the most favourable circumstances, pain, swelling, and congestion may affect the region of fracture for several days. One or other region of the body may be rapidly frozen: the inflammation does not manifest itself till after the physical agent has ceased to act, but it continues for hours, and even for days.

There are, moreover, physical irritants of another nature producing

definitely chronic inflammation; I refer to foreign bodies which have gained an entrance into the system. These if bland in themselves may nevertheless cause irritation. A good example of the extensive inflammation which such bodies may set up is seen in the dense fibrous interstitial tubercular masses developed in the lungs of stone-masons around fine silicious particles carried into the lymphatics from the alveoli.

From such examples it will be evident that no satisfactory distinctions between bacterial irritants on the one hand, and physical irritants on the other, can be founded on the duration of irritation. This factor plays no easily recognised part in determining the various forms of inflammation, and consequently I have forborne to place it in the list at the beginning of this chapter.

In thus passing rapidly over the influence of each of the four main causes of variation I have of necessity excluded sundry forms of inflammation due to the combined action of two or more. There are, for instance, such well-marked forms as the catarrhal and croupous, due to the interaction of all four factors: embolic inflammation and lymphangitis have also been passed over; these, however, are not so much forms of inflammation as inflammatory processes occurring in special regions as a result of special methods of conveyance of the irritants.

The factors then are so many, and their interaction so varied, that anything approaching to an orderly classification is hopeless. What I have here written must be regarded, not as an attempt to formulate such a classification, but as an attempt to indicate briefly how the nature and position of the tissues, and the nature and intensity of the irritant bring about modifications in the process of inflammation.

Chapter 2. — On Systemic Changes Consequent upon Inflammation

The results of an acute local inflammatory process are not confined to the immediate locality, but associated alterations in the system at large have long been recognised; yet while recognised these systemic changes have been but little studied: I cannot pass the matter over in silence, but my setting forth of it must necessarily be very brief and imperfect.

I cannot here say more upon the effect of local irritation on the nervous system than that, apart from direct reflex action leading to changes of nervous origin in the region of injury and the reflexes affecting associated regions, the higher centres, and through them the system at large, may become affected by paths that it is not always easy to trace.

The disturbances of the nervous system which accompany local injury can be but vaguely and indefinitely described. As regards the secondary effects, the recent most suggestive work of Prof. Roy and Dr. Cobbett upon *Shock* [*vide* art. on "Shock" in a later volume] indicates that there is here a rich field for yet further research. Of the changes in the general circulation, and more especially in the circulating blood, thanks to the

observations of Von Limbeck, Rieder, Löwitz, and Sherrington, we are in possession of more exact knowledge. On acute local inflammation of some extent the circulating blood becomes inspissated; by exudation it loses some of its plasma, while the more solid constituents — the red corpuscles — do not escape. The amount of fluid lost to the circulation is not equalised by increased entrance of lymph into the circulation: in one experiment of Prof. Sherrington the blood remained apoplasmic (*i.e.* its specific gravity remained heightened) for more than sixty hours after the infliction of injury. This apoplasmia or diminution in the relative amount of plasma in the blood appears to depend in some measure upon the extent of the vascular area involved in the inflammation; for example, Sherrington shows that when both feet are involved, by plunging the limbs in water of 52° C., the apoplasmia is more severe than in experiments affecting one foot only. Another well-marked change in the blood concerns the leucocytes. As suspected by Löwitz and proved by Sherrington, there is, in some forms of inflammation at least, a primary diminution in the number of leucocytes per unit volume of blood (leucocytopenia), followed by a marked increase in the number of leucocytes in the blood (leucocytosis). The number of leucocytes was in some instances increased sevenfold. In the leucocytopenia of inflammation, the diminution is chiefly confined to the finely granular leucocytes — the finely granular oxyphile cells of Kanthack and Hardy. These observations of Sherrington are confirmed by the observations of Everard, Demoor, and Massart.

Whether the diminution be due to disintegration, or to collection in some area of the circulation, is not yet determined. The leucocytosis may become obvious within an hour after the establishment of a local lesion; and it may be prolonged for several days, even in cases where the injury has been of a mechanical nature. Here, again, according to most observers, it is chiefly the polynuclear or finely granular oxyphile cells which increase in numbers. It is interesting to note that coincidently the coarsely granular eosinophile cells appear to undergo great diminution. I can do no more than point out the existence of those blood changes, and further that changes in the number of leucocytes in the blood are certainly not accounted for by the number passing from the blood into the inflamed area. It would seem that local inflammation in some way brings about an over-stimulation of lymph glands, whereby an increased number of leucocytes are poured into the blood; or it may initiate increased proliferation of the leucocytes already in the circulation; but how one or other of these effects is produced is at present unknown. Certainly the direct introduction of the products of bacterial growth into the circulating blood may lead to a more or less pronounced and rapid diminution of the number of leucocytes in the blood, and this diminution, as shown by Löwitz, may be preliminary to a subsequent increase.

The further important general disturbance associated with local injury, more especially when of bacterial origin, namely, the occurrence of fever, will be described in another article. Bacteriological studies

lead to the conclusion that traumatic fever, at any rate, is largely due to the diffusion in the blood stream of soluble bacterial products, and of the products of tissue destruction derived from the inflammatory focus.

Chapter 3. — Conclusion

In studying thus the reactions of the organism to injury, we are impressed by the multifariousness of natural processes; the end may be attained not in one way only but in many. "It is not by cells of one order alone — by phagocytes — or by leucocytes in general and only leucocytes, or merely by the reaction on the part of the fixed cells of the tissue, or by vascular changes alone, or by altered temperature, or solely by the chemical and mechanical action of the exudate that repair is effected. All means are employed to antagonise the irritant and to effect healing. The cells of the body, fixed and free, play their part; the nervous system aids the process; the bodily humours render efficient help; modifications in the vessel walls and blood stream are valuable auxiliaries. Diverse processes are employed, now one more particularly, now another, according to the needs of the moment, but none exclusively."

The time has come when, example after example having clearly indicated the meaning and the tendency of that response, we may securely acknowledge the tendency, and see in inflammation not merely the response to injury, but the attempt to repair injury. To object that a definition containing this statement is teleological is absurd in the face of fact after fact that can be interpreted on this assumption only. What is the development of cicatricial tissue but an attempt at repair? What other meaning can be ascribed to the increased bactericidal power of the inflammatory exudate as compared with that of ordinary lymph and blood serum? Why do leucocytes accumulate in a region of injury? Why do some of them incorporate bacteria and irritant particles, and others bring about the destruction of these without necessarily ingesting them? All these are means whereby irritants are antagonised or removed, and reparation and return to the normal sought after.

It must be kept in mind that attempt to repair may be far from repair. Indeed, we frequently find that the reaction to injury is disproportionate to the strength of the irritant, being either insufficient or excessive. The exudation may possess but slight bactericidal powers, or may be poured out in such quantities that the microbic irritant, instead of being retained in the region of injury, is conveyed outside that region; the wandering cells instead of destroying, may undergo destruction; they may incorporate bacteria, but not be able to annihilate them; the fixed cells may either form an incomplete cicatrix, or continue to proliferate in excess. The means of defence on the part of the organism are not so much a preparation in advance as an inheritance or an acquirement — either a transmission from those forms which, being possessed of the most highly developed means of defence, have survived while forms with fewer resources have been destroyed; or, on the other hand, an accession derived

from previous successful resistance: not being a preparation in advance, the reaction to injury is not exactly proportionate to any and every irritant.

But the mere statement that inflammation is an attempt to repair injury, or that it is the response thereto, is insufficient as a definition, for thereby the general disturbances which may accompany the changes occurring at the seat of lesion are included; these, however, may be excluded without seriously affecting our conception of the process, in fact with positive advantage to a clear comprehension of the distinction between inflammation and fever. And, further, if what I have urged in the chapter upon the part played by the nervous system be correct, account must be taken of the fact that the leading phenomena associated with the inflammatory process may occasionally present themselves solely under the direction of perverted nerve action, and apart from actual local injury.

Hence I am inclined to consider that we can now pass beyond the conception of the process with which I began this article, and cannot merely regard it as a succession of changes in a part constituting the reaction to injury, but can with propriety acknowledge the purpose of that succession. From these considerations I am led to define inflammation *as the series of changes constituting the local manifestation of the attempt at repair of actual or referred injury to a part, or, briefly, as the local attempt at repair of actual or referred injury.*

So diverse are the opinions of pathologists upon many branches of this subject of inflammation, and so great is the amount of recent research that I can neither hope that all the conclusions here set down will gain acceptance, nor that in these pages, inevitably condensed as they are, I have succeeded in recognising and duly acknowledging all work of primary importance. It is possible also that, having been unavoidably prevented of late from seeing and discussing with others the results they have obtained, I may in some cases have viewed facts in a wrong perspective. In the rapid progress of our science, much, it may be, that is here set forth will be modified. Nevertheless I hold that the conception of the inflammatory process indicated in this article is that which embraces the largest number of like phenomena, and excludes most satisfactorily those which if associated are unessential; and that it is by the study of cellular pathology in its strictest sense that the surest advance has been and is to be made in our knowledge of this the dominating process in disease.

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THE DOCTRINE OF FEVER

This essay is divided into two parts. In the first, which is introductory, the subject is treated in the order of time. Beginning with Virchow an account is given of his doctrine of Fever; then follow the doctrines of his most distinguished contemporaries and successors in the field of Pathology — Traube, Liebermeister, Senator, Leyden, Cohnheim. The second part, entitled "Recent Researches," relates to the years which have elapsed since Cohnheim's death in 1874. The aspects of each branch of the subject of Fever are dealt with under the following heads: — Disorder of Nutrition, Thermogenesis, Pyrexia, Cerebral Heat-Centres, Antipyretics, Ætiology.

In a concluding section I have endeavoured to set forth that view of the nature of Fever which, in my judgment, harmonises best with our present knowledge of the subject.

Part I. — Historical Retrospect, 1850–1883

Of the scientific conceptions relating to the origin and nature of diseases, out of which the science of pathology, as we now understand it, was built about fifty years ago by Virchow and his immediate predecessors, none were more fundamental than those relating to fever and inflammation. These conceptions were so entirely unconnected with the theories which had previously been taught under the name of

General Pathology that, in tracing the development of our present knowledge, no advantage would be gained in going farther back in our retrospect than the middle of the present century.

Johannes Müller — whose teaching was the spring of the great movement in all matters relating to the nature of disease, of which Virchow was the exponent — had compared fever to a reflex process of which the phenomena were the response to stimulation of the spinal cord by means of "organic nerves." About the same time the discovery by E. H. Weber of the inhibitory nerve of the heart had suggested new ideas as to the way in which the central nervous system governs the circulation. He had shown that this influence is exercised, so far as the heart is concerned, by two channels of which the actions are antagonistic, that of the one exciting, that of the other quelling. As regards the blood-vessels, constricting or tonic nerves had been discovered, but it remained for Schiff to find out that there are also nerves which control vascular tone.

Out of the principle of antagonism which the discovery of Weber involves, there developed in the fertile mind of Virchow the notion (he declined to call it a theory)[1] of *fever as a neurosis*, which was expressed in his treatise on Pathology published in 1853. Students of pathology were taught by him for the first time that fever was not an over-activity, but a paralytic state; that its excesses — the over-action of the heart, the "tension of the whole vascular system," "the abnormal production of heat" — were the expression of *failure of control*, of weakness rather than strength. But of the way in which this control was exercised, or how it failed, he could at that time give no explanation; he contented himself with suggesting that the "moderating centres" could influence not merely the heart and blood-vessels, but also the "*Stoffwechsel*," what we now call metabolism. According to Virchow, the nervous system in fever loses its control over all the organic processes, and in this the essence of the febrile state consists.

In 1855 Traube (1) made the discovery that in fever *the elimination of nitrogen is increased*.[2] The fact seemed to indicate that if fever be a neurosis, there must either be "trophic nerves" by which the chemical processes of the organism can be controlled — for how else could an affection of the nervous system bring about tissue disintegration? — or we must suppose, as did Dr. Parkes, that the cause of fever, the catalytic agent of which Virchow wrote, directly attacks the tissues. Traube's explanation, however, differed from both of these, for he thought that the admitted increase of disintegration of albuminous compounds was secondary to the disturbance of the circulation. Of the nature of this disturbance he framed a theory which, whether true or not, exercised a greater influence than any other on the progress of investigation. It may

[1] "Das Alles ist gewiss sehr wenig und genügt auch nicht annähernd um eine Theorie darauf zu bauen." — Virchow, *Handb. der Pathol.*, p. 36.

[2] It is noteworthy that the paper in which this discovery was made known is one of three pages.

be shortly stated as follows: — Traube, like Virchow, assumes the existence of a fever-producing agent, but holds that its action is exercised, not on inhibitory, but on tonic vaso-motor nerves; that the first physiological result of this influence is contraction of the peripheral arterioles, and consequently a rapidly diminished flow of blood to the surface; the temperature of the skin declines, and a rapid rise of internal temperature follows. To the increase of the difference between the external and internal temperatures he attributes the rigor of accession. The decline of temperature is due to nothing more than the cessation of the vascular spasm. So hard and fast a statement of what happens in fever was found difficult to accept; and it soon appeared that it was not in accordance with observation. In the initial stage its utility as a "working hypothesis" consisted in this, that it gave prominence to the influence of the nervous system on the liberation of heat at the surface, and to the adjustments by which this liberation is adapted to the requirements of the organism; thus investigation was guided in a direction which the event has proved to be the right one.

Liebermeister was the first pathologist who attempted to investigate fever calorimetrically, the outcome of his work being firstly to demonstrate that even when the surface loss is entirely annulled by raising the temperature of the environment to such a point that no heat is parted with, the increase of bodily temperature is not so rapid as in the initial stage of many fevers; and that, consequently, the latter could not be explained on Traube's principle; secondly, to give prominence to two doctrines of his own, which for a long time were very generally accepted. Liebermeister's doctrines were — (1) that in fever, as in health, constancy of temperature is ensured by the adaptation of production to discharge, not of discharge to production, as Traube taught; and (2) that in fever bodily temperature is regulated in the same way as in health, with this difference that the norma has become several degrees higher. In fever the organism, according to Liebermeister, strives not towards the temperature 98·6° F., but towards 104° or 106°, as the case may be. Liebermeister's inference from his experiments, that arrest of surface loss is inadequate to produce pyrexia, will not, as we shall see, bear experimental criticism. To the theory stated above much greater interest attaches, because if illogical in form, it conceals an important truth. An abnormal norma may be a contradiction in terms, but the fact that the bodily temperature in continued fever approaches a certain limit which it does not tend to exceed, is one which will not be disputed.[1] Its meaning, however, will be more advantageously discussed in a subsequent paragraph.

[1] There are many distinguished pathologists who still hold to Liebermeister's doctrine that in fever the temperature is adjusted to a new norma. The facts which seem to support it may be exemplified in the following experiment: —

It is possible either to raise or to depress the temperature of a healthy person by gradually cooling or warming the water of a warm bath in which he is placed. If by this means you depress the temperature of his body as much as ½ degree F. he shivers, if you raise it to the same amount he perspires. Repeating the experiment on a fever patient

At this point the subject was taken up by Senator, the most successful, if not the ablest, of all the investigators of fever. We have seen that although Traube and Liebermeister differed very widely in their views, they agreed with Virchow in regarding fever as a disorder of that function of the nervous system by which constancy of temperature is maintained — the function of thermotaxis. Traube, being both a physiologist and a physician, was guided by the application of physiological inferences to clinical facts, Liebermeister very largely by observations relating to the treatment of fever by the tepid bath. Both recognised regulating centres, but as regards the way in which they act their views were antagonistic; the one relied on vaso-motor nerves, the other on the control of heat-producing chemical processes by the nervous system. To Senator it appeared that the time had come for investigating the subject from all sides, experimental and clinical. Fever comprehends vascular, thermal, and metabolic phenomena, and no investigation seemed likely to be of value unless all three were dealt with.

In the laboratory, Senator compares for the first time the discharge of heat of animals in which fever had been produced artificially, with the previous heat loss of the same animal and with the heat loss after recovery, employing, at the same time, the best methods then available for measuring the respiratory exchange and the elimination of nitrogen. One of the most noteworthy results was that, while the nitrogenous waste was considerably increased, there was no increase whatever of the consumption of fat, and no evidence of any greater increase of the respiratory exchange than could fairly be attributed to the existence in fever of conditions more favourable to the discharge of carbonic acid gas.

As regards the discharge of heat, measured calorimetrically by a method far more accurate than that of Liebermeister, the results were negative. In the initial stage the surface heat loss appeared to be diminished, but it could be ascertained that this diminution was compensated later. In respect of the discharge of nitrogen, Senator's clinical observations confirmed and extended what had previously been observed, and showed in this respect a complete correspondence between natural and artificial fever. He estimated the rate of elimination of nitrogen in many instances to be more than double, *i.e.* to be increased in a degree out of all proportion to any increase which could be supposed to take place in the rate of heat production.

At the time that Senator published his *Researches on the Process of Fever* (1873), Leyden was engaged in clinical investigations of the same subject (4), with results which differed from Senator's in some points of importance. The absence in animals of any marked increase of the

you obtain a similar result, with this difference, that if the temperature is say 104° F., he shivers at 103·7° and perspires at 104·3°; whereas the healthy person, whose normal temperature is 98·8°, shivers at 98·3° and sweats at 99·2°. The explanation is that it is the change of temperature that produces the reaction, and the direction which determines its character — shivering if it is descending, sweating if it is ascending.

respiratory discharge of water and carbon dioxide had led Senator to conclude that in fever the only essential change in metabolism relates to the increased disintegration of proteid. On this point, however, Senator was for the most part guided by experiments on animals. Leyden, therefore, directed his efforts to ascertain the condition of the respiratory exchange and thermogenesis in man. Considering that in continued fever there is no obvious indication of increased thermolysis, it was desirable to test this by more exact observation. For this purpose he employed a method of calorimetry which can be used clinically without inconvenience to the patient. Enclosing a limb in a cylindrical calorimetrical chamber, he estimated the loss of heat by escape of water, evaporation and radiation of the limb in relation to the surface, and calculated therefrom the whole surface-loss of the body, with the result that in fever, even when there is no visible perspiration, the thermolysis may be 40 per cent greater than in health. Having arrived at this result by clinical observation he had recourse to experiment (5), in the hope of confirming it by investigating the respiratory exchange in animals. The result was that in all cases the rise of temperature was accompanied by a corresponding increase of the discharge of carbon dioxide, the amount and duration of which was such as to preclude the possibility of attributing it to the greater activity of the respiratory movements. Shortly after the completion of these observations a series of experiments were made under Pflüger's direction (6), in which both the oxygen intake and the output of carbon dioxide in normal and fevered animals were compared. These led the great physiologist to incline to Liebermeister's view, that normal regulation consists in the adaptation of production to discharge, and that increased production is an essential element of fever.

By way of conclusion to this retrospect I propose to state summarily how the question of fever presented itself to the two pathologists most competent to discuss it, — Senator and Cohnheim.

Cohnheim, like Pflüger, in the Lecture on Fever which concludes the second volume of his *General Pathology*, sums up in favour of the doctrine that the nervous system presides over thermogenesis no less directly than over thermolysis. He accordingly seeks for evidence of increased production of heat throughout the whole febrile process.

In the initial stage, particularly when the rise of temperature is rapid, he admits that the cutaneous circulation is restricted, but not that this restriction is the cause of the rise. The sensation of chill is due to the suddenness of the diminution of temperature at the surface: when the change occurs gradually, it is absent. It is succeeded, in the fastigium, by a feeling of warmth which means that the constricted vessels relax. He leaves undecided whether this is due to the intervention of inhibitory nerves or not, but emphasises the fact, as evidence of vaso-motor disturbance, that the more favourable state of the cutaneous circulation which characterises the beginning of the fastigium is liable to interruption by

the recurrence of chills, in which the skin becomes dry and the temperature tends to rise. The critical sweating is of course regarded by Cohnheim as a sign of increased flow of blood to the surface, which he does not hesitate to attribute to the influence of dilating nerves. Of cutaneous nerves of secretion little was known at the time when he wrote.

The remarkable fact that in fever the diurnal range of variation is much greater than in health, Cohnheim attributes rather to fluctuations in thermogenesis than to changes in the circulation. This view seems to him supported by the consideration that in relapsing fever the efficient cause of pyrexia is plainly the presence of spirilla in the blood, and that these would influence thermogenesis rather than surface loss. Had he known how close is the relation between the successive stages of ague and the life history of the organism which causes it, he would have been confirmed in his conclusion that in periodical fevers the periodicity is a function of the cause, not of the disease.

In common with Virchow and all modern pathologists, Senator regards fever as a disorder of temperature regulation, but for him the term regulation connotes "regulation by the cutaneous circulation." It is thermolysis, not thermogenesis, that is in the first instance disordered. This disorder is most marked in the initial stage, but exists in the fastigium, declining towards its close. Its presence manifests itself in dryness of the skin and maintenance of the high temperature, but of these two neither is caused by the other; both are directly dependent on the nervous system.

Finally, Senator regards the relation between the constituents of fever as a loose one: he believes there is no absolute inter-dependence of the disorder of nutrition and the pyrexia. The only invariable causal relation is that which subsists between pyrexia and disorder of the cutaneous circulation.

Part II. — Recent Researches

1. The Disorder of Nutrition in Fever. — (*a*) *The Respiratory Exchange.* — When, after a pause of several years, the investigation of the febrile exchange of material was resumed both from the clinical and the experimental side, the new methods for measuring the normal exchange which had in the meantime been devised, and the discoveries they had rendered possible, afforded to the pathologist advantages which he did not before possess. With reference to the gaseous exchange particularly, the apparatus devised by Professor Zuntz had rendered it possible to measure the oxygen intake and the discharge of carbon dioxide in man for very short as well as for longer periods, with an accuracy which had before been attainable only in investigations on small animals; and by this means very important new information had been obtained as to the respiratory exchange in man, particularly by Lehmann and Zuntz's experiments on the fasting men Cetti and Breithaupt. It was under these

conditions that Dr. F. Kraus, using the same apparatus and method, entered on his investigation of the respiratory process in human fever, his aim was to obtain data relating to the febrile exchange of gases in such form that the rate of discharge of carbon dioxide and that of the oxygen intake should be determined at short intervals, and that, in order to secure constancy and uniformity as regards the state of nutrition of the patient, each period of observation in fever should begin at a sufficient interval of time (sixteen hours) after the last meal, and be repeated in convalescence. The general result of this inquiry was that in all cases of acute fever there is increase of respiratory activity (*i.e.* greater frequency and depth of respirations), and that, whenever this is the case, the actual intake of oxygen is increased, but that when the febrile state is prolonged this effect soon subsides, notwithstanding the continued abnormal elimination of nitrogen. It was further found that in man, as in animals, the respiration quotient $\left(\frac{CO_2}{O}\right)$ remained unaltered. As regards the degree of augmentation of both factors the results were in satisfactory accordance with those yielded by observations on artificial fever. They were further confirmed by a subsequent series of observations on the febrile state induced in tuberculous patients by the use of tuberculin. The observations of Dr. Loewy in the Charité and Moabit hospitals at Berlin were made in the same way, with perhaps even greater exactitude, and particularly with more careful attention to the state of the patient and the stage of the disease. The results differed in some respects from those of Kraus, but the differences were of little moment. Thus it was found that although there was usually augmentation of the oxygen intake with or without increase, depth, or frequency of respiration, this was only observed when the temperature was actually rising; so that Dr. Loewy was led to regard this effect as a character of the initial stage, and to associate it with the shivering of the skeletal muscles and the increased tone of the vascular muscles which are the concomitants of this stage.

In many cases the respiratory quotient remained the same; but in others there was a diminution, which might have been regarded as a consequence of the febrile state had not the general principle which serves as the pathologist's guide in all investigations relating to febrile metabolism been attended to, namely, that the comparison of the pathological state with the normal, as a guide to the correct interpretation of the results, can only be relied upon when care is taken to compare data relating to the same individual at different times; or, if this cannot be done, to make the comparison between normal and fevered individuals in the same physiological conditions as regards nutrition. The exact observations already mentioned by Lehmann and Zuntz (9) as to the two fasting men afforded the information. By comparing Loewy's results with theirs, it is seen that the diminution of the respiratory quotient which he observed in his fever cases was normal for a person on fever diet.

The general result is that in man the respiratory exchange is not materially altered in fever either in quantity or quality, and that when it

is increased the increase is not to be regarded as an essential character of the febrile state, but rather as an effect of some abnormal form of muscular activity. Comparing this statement with the experimental results obtained by Liebermeister, which led him to believe that in the initial stage the respiratory exchange was often doubled or trebled, the reader will at once see that the key to the apparent discrepancy is to be found in oxidation processes which are associated with muscular contraction, but have only a secondary connection with fever.

(*b*) *The Discharge of Nitrogen.*—The fact that the rate of discharge of nitrogen by the kidneys in fever is equal to or even greater than that which prevails in health, notwithstanding that the intake of nitrogen is reduced to a minimum, has been long familiar to pathological students. First discovered and made known by Traube (10) in 1855, it was investigated clinically by Ringer in 1859, experimentally by Naunyn (1870), Senator, and many others. It has also been long known that on the whole the elimination of nitrogen runs with the temperature (Huppert, 1866) (12); that the daily discharge is often more than double what it would be in a healthy person on fever diet; that although the increase of nitrogen elimination begins, as was observed by Ringer, before the temperature rises, the rate of elimination is greatest, not during the initial stage, but at an early period in the fastigium, and finally that defervescence is often followed by an epicritical increase.

The discharge of nitrogen affords much plainer indications in fever than the respiratory exchange; it unquestionably denotes that proteid material is being disintegrated; and the rate at which this takes place can be easily estimated from that of the discharge of nitrogen. The fevered, like the starved organism maintains itself on its own proteid and fat. It discharges nitrogen by the kidneys, carbon chiefly by respiration. Modern methods of research enable us to determine the rate of both discharges with exactitude, and thereby to ascertain how much proteid and how much fat the organism uses per hour or day for its maintenance. Such investigations are required, not for the purpose of confirming the well-established observation that in fever disintegration of proteid is increased, but with a view to the much more difficult question whether the febrile disorder of metabolism is of the same nature as that which occurs in inanition, and is dependent on the inability of the individual to take nourishment, or is partly or wholly the result of some change in the living substance of such a nature as to render it more prone to disintegration. As already indicated, the only way to answer this question is by comparing the exchange of the fevered individual with that of the normal man who abstains from food, or of the animal which is deprived of it. In animals the comparison can be made with a degree of exactitude which cannot be approached in man. The method to be followed, therefore, consists in first ascertaining with precision what happens in artificial fever, and then using the data so obtained as a basis for our observations on man. And it is important to notice that in relation to a question like the present, the common objection that

the processes of nutrition in a small rodent cannot be applied to man does not hold. If our object were to obtain data for a general view of the whole process of nutrition in man, those furnished by observations on the rabbit, for example, would be inadequate. But the question now before us is much more elementary. If it can be shown that fever can be produced in the rabbit, and that it is accompanied by a disintegration of proteid which is obviously of the same nature as that which we observe in man, we are justified in using the precise knowledge which the experimental method affords us, as a key to the interpretation of clinical observations made under circumstances less favourable to perfect accuracy. As regards the rabbit it has been further, and with much more reason, objected that its nutritive process is subject to irregularities which it is difficult to account for, and which unfit it for observations the value of which depends on the constancy of the observed phenomena. But even this objection admits of an answer; for it has been found that, in animals deprived of food, a condition is very soon reached in which the discharge of nitrogen becomes constant. This constancy obviously denotes that the nitrogenous material derived from the food last taken has been used up.

In inanition where, as has been said, the organism feeds upon itself, the ordinary process of life is so modified that tissue no longer maintains its integrity. It wastes, and by wasting supplies the material for the maintenance of systemic life. In the rabbit this waste is sufficiently constant for the purposes of investigation. Thus Dr. May in his recent research on the exchange of material in fever, found that in eight rabbits on the third and fourth day of inanition, the daily discharge of nitrogen was (with little variation) 0·055 per cent of the body weight: it could be assumed, therefore, with certainty that when, by inducing fever, this amount was increased — *e.g.* to 0·066 per cent — this increase was due to exaggeration of the normal elimination of nitrogen. That in fever, as in inanition without fever, the increased discharge of nitrogen represents disintegration of tissue can scarcely be doubted; but the immediate cause of this disintegration admits of discussion. In the absence of disease, if I may so express myself, the tissues of the starved body yield to necessity. Sugar, derived from the digestion of amylaceous food, being no longer available for the maintenance of respiration, proteid goes to meet the inexorable requirements of the organism. In fever there is no *prima facie* reason for supposing that a new process is brought into existence, or that the state of things is not the same as in inanition. But the question cannot fail to suggest itself whether in fever the organised material is more labile than it is in health, *i.e.* that the direct injury which it receives from the fever-producing cause (the nature of which will be discussed later) renders it less able to resist the demand of the organism. The grounds for this very generally accepted assumption are as regards the initial stage of fever not very substantial. Eventually the living material of the body no doubt suffers from the continuance of high temperature and defective nutrition; but there is no reason for supposing that this damage is the precursor of the general disorder. In favour of the opposite

view — namely, that the disintegration is essentially dystrophic — there are several arguments. If the proteid disintegration of fever were of a different nature from that of inanition, we should expect that the products would be different. It has indeed been suggested that the presence of acetone in the urine in febrile diseases indicates that is so; but the investigation of the cases of voluntary starvation (Cetti and Breithaupt) by Lehmann and Zuntz have shown that acetonuria belongs as much to inanition as to fever. We know also that this condition is an accompaniment of many wasting diseases (particularly cancer) in which fever is absent. Another reason for the same view is that in fever the nitrogenous waste can be diminished by a suitable diet. In fever glycogen disappears from the liver, and cannot be replaced by the administration of amylaceous food: this obviously means that the supply of carbohydrate in the organism is exhausted early, and that in consequence the organism begins almost at once to feed on itself. This consideration led Dr. May to make experiments for the purpose of ascertaining whether in his fasting rabbits the extra consumption of proteid could be prevented by the administration of grape sugar, *i.e.* of a carbohydrate ready for immediate metabolism. In an inanition without fever the diminution of nitrogenous waste was immediate, and amounted to 25 per cent. In fever it was about the same, showing that the febrile waste may, in the first instance, be entirely dystrophic. It is a question for clinical observation whether in the human subject good might not be done by following out the same principle.

2. Production of Heat (Thermogenesis). — To some readers it may appear superfluous to inquire whether thermogenesis is increased in fever; for it might seem to follow from the increased temperature of the body that more heat is produced. A moment's consideration will, however, convince any one who is willing to take the trouble to reflect, that constancy of temperature depends not on the quantity of heat generated by the consumption of food, or on the quantity lost at the surface, but on the power which the organism possesses of so controlling either production, or loss, or both, that the normal temperature shall not fluctuate in either direction. In fever it cannot be questioned that this power of control is so impaired or weakened as to make it inadequate for its purpose; the way in which this is brought about will be considered in the next paragraph. What we have now before us is the fact that in fever the production of heat is on the whole somewhat increased and the reason why it is so.

It is now nearly thirty years since Frankland determined, by a series of calorimetrical experiments made at the Royal Institution, the "heat values" of the chief constituents of food. These data, combined with what was known or could be ascertained as to the quantities of each constituent consumed daily in maintaining the animal machine, enabled physiologists to estimate approximately the total quantity of heat consumed therein in a day or an hour. The endeavour was made at the same time, by the employment of calorimetrical methods, to measure the

same quantity directly. The results of these early efforts have given place to more precise ones, for we are now not only able to state the heat values of the various nutritive substances with much greater correctness than before, but are able to measure with like precision the quantity of heat which each substance actually produces physiologically, *i.e.* when it is consumed by the organism as food, and to show that the two values agree. It is also found that the total heat production of the body in a given time, as measured directly, equals the sum of the heat values of the various substances consumed during the same period. We have therefore in our hands the experimental proof of what Mayer told us half a century ago, namely, that food is the sole source of animal heat. The production of heat in fever must be estimated in the same ways as the production in health, *i.e.* either by determining the quantity of each nutritive material used, and adding the corresponding heat values, or by direct calorimetrical measurement. In fever the organism consumes, as we have seen, its own proteid and fat. The data and methods which we now possess render it possible, as is well exemplified in Dr. May's research, to estimate the rate of each of these processes of consumption in fever, and to compare the results obtained under the same nutritive conditions in health. By such comparison it was found, in the rabbit, that the fevered animal produces and discharges something like ten per cent more heat than the healthy under the same conditions of nutrition, and that this is due, not to the disappearance of fat, but to the consumption by the fevered organism of its own proteid; for, while the consumption of fat is approximately the same in both cases, the nitrogenous waste in fever is about 25 per cent greater.[1] In another recent research, in which the excellent calorimetrical method of Professor Rubner was used, the maximum increase of heat production in fever was determined under the same conditions and on the same animal by direct measurement. The result thus obtained closely accorded with the estimate founded on the quantities of proteid and fat consumed. The increase never exceeded 10 per cent, but was often less, and in some experiments was so inconsiderable, that the author was unable to say more than that while in the rabbit there may be an increased production and discharge of heat in fever, the possibility of fever without such increase cannot be excluded (14).

3. Pyrexia. — We now come to the most important part of our inquiry. Why does the bodily temperature rise above the normal? I have already explained why the dictum of Liebermeister, that in fever the organism is adjusted to a higher normal, cannot be accepted as it stands. The truth which it encloses may be expressed by saying that, in consequence of the injurious action of the fever-producing cause, the organism loses its power of keeping itself at the normal temperature. In this very modified form Liebermeister's principle is now accepted by all pathologists. All that is asserted is that the organism possesses and exercises the power of adapting its temperature to a norma, that norma

[1] See p. 57 of Dr. May's paper. I much regret that space will not allow me to give details.

being the temperature which is most conducive to its own interests, and that this power is impaired in fever. It leaves untouched two other inquiries, viz., (1) in what part of the organism the power is vested, and (2) why the departure from the normal moves upwards and not downwards. Let us consider these two questions separately.

It is conceivable that in an organism consisting of cells, all of which are similar to one another in physiological endowment, *i.e.* without a nervous system, each cell might be able to govern its own chemical, *i.e.* heat-producing processes, in such a way as to maintain a constant temperature; but this could only happen if all of the cells were under the same conditions, *i.e.* inhabited the same environment. Identity of endowment without identity of environment would not bring about the required result, viz., identity of temperature. It need scarcely be said that though conceivable, no such organism is possible. Constancy of temperature is met with only in animals of advanced organization and highly-developed nervous system; and in them constancy of temperature presents itself exclusively in internal parts. Of external parts the temperature is variable. The circulation affords an efficient mechanism by which outside variability is used for the maintenance of inside constancy. In other words, such a relation is kept up by the circulation between surface and interior as to ensure equability of the latter. The existence of such a relation implies the agency of a nervous system to maintain it. It therefore needs no experimental evidence to prove that to this system must be assigned the "thermotactic" function. This being admitted, we may go a step farther. From what we know of the mode in which the nervous system co-ordinates functions, it may be assumed that thermotaxis is conducted by a "centre" or "centres"; that it or they receive impressions of "too warm" or "too cold" by afferent channels in those parts in which it is their business to maintain constancy, *i.e.* normality; and that they (the centres) are able to influence "thermolytic" or thermogenetic processes accordingly. The organism, represented by the "centres," recognises as normal the temperature which in the phylogenetic development of the species has established itself as most advantageous. If, therefore, we speak of impairment of thermotaxis, we mean that the centre loses its power more or less of responding to impressions of abnormality in the parts with which it is in relation by afferent channels. If so, why does the defect show itself in one direction only? If fever implies paresis of the regulating centre, why does the temperature rise, never fall? To this there is but one answer, and that a very simple one. A good horse needs the bridle only, not the whip. The heat-producing activities of the organism tend to exceed, not to fall short of its requirements. So long as this tendency is operative, pyrexia must result from mere impairment of the regulating function. It is not until it ceases, as happens in many instances as death approaches, that fever becomes collapse (26).

So far we may proceed independently of experimental evidence. In approaching the question which next presents itself — the question where

the thermotactic centre or centres are to be found, and how they act in fever — we may, I think, take as our guide the principle that, whatever the agency which in health prevents the temperature of the body from rising above the normal, it must be that agency which in fever is disordered. If so, the question how this control is normally exercised — how the organism deals with its surplus production, is one of great pathological interest. The best way of answering it is by another inquiry. How does the organism deal with increase of surplus, when the increase is dependent on conditions which are not those of disease? There are two such conditions — food and exercise — both which are under the control of the will. In the fasting animal the effect of feeding is to double or treble thermogenesis. By muscular exertion it may be increased in somewhat similar proportion. The storage of heat and consequent increase of temperature in either of these two cases would be disastrous, were the latter not promptly got rid of by some arrangement of unfailing efficiency. In the case of food it is conceivable that the organism might be able to protect itself by putting a stop to the thermogenetic chemical processes to which the taking in of food gives rise; but there is no way in which the heat produced by muscular exertion could be so dealt with as not to increase the temperature of the body other than increased liberation of heat at the surface. The physiological processes which are connected with the discharge of heat at the surface are presided over by two systems of nerves (secreting and vascular) which are closely associated with each other functionally and anatomically. The secreting nerves which are distributed to the sweat glands, and the inhibitory vascular nerves by the stimulation of which the minute arterioles of the skin dilate so as to increase the vascularity and heighten the colour of the skin, come from centres which are situated in the bulb and spinal cord. The two systems of nerves follow the same lines and are very similarly distributed. That the dilating nerves and hidrotic nerves are very prompt and efficient agents in guarding against increase of temperature can hardly be doubted, for in all known instances in which the temperature tends to rise they at once manifest their activity. In fever this activity fails; considerations which we have already had before us suggest that this power of responding is still present, but is impaired. We have now, with a view to this hypothesis, to inquire how far it is supported by clinical observation and experiment as to the phases of the cutaneous circulation and of the secreting function of the skin. In this inquiry we shall have to do, not with production and discharge, but with the behaviour of the vessels and glands, and with the centre or centres by which they are regulated.

When the accession of pyrexia is marked by rigor the skin exhibits the conditions which were regarded by Traube as belonging to the whole process. It is obvious that in many fevers, particularly ague, there is in this stage of accession "spasm of the extreme vessels"—anæmia of the skin. This is followed by an opposite condition which, although neither so marked nor so constant as the previous pallor, is by contrast sufficiently obvious. If, at the beginning of the fastigium the surface

be exposed, rigor is apt to return, as if the shuddering contraction of the muscles were a reflex evoked by the cooling of the skin.

Whenever pyrexia ends in a distinct crisis, *i.e.* a sudden return of the bodily temperature to the normal, that return has associated with it changes in the skin still more favourable to the discharge of heat; eventually it resumes its normal condition, but before doing so the circulation becomes more active and sweat breaks out abundantly. Thus in typical fevers we have two states which are easy to appreciate — the anæmic dryness of rigor and the warm, hyperæmic moisture of defervescence. Between the two comes the fastigium, during which the vascular condition, even if not markedly hyperæmic, is abnormal and variable. Of this we have plain indications in the observation that even rough measurements of the surface temperature show such differences between corresponding parts on opposite sides of the body, and between the temperatures of the same part at different times, as are never observed in health. This is further shown by the abnormal way in which the skin responds to stimulation. In prolonged fevers, particularly typhoid, it is observed that if a pencil is drawn firmly over the skin the path it has followed becomes after a few seconds traceable by its relative paleness. This blanching lasts for several minutes, spreading slightly as it fades. In animals the evidence that the cutaneous vascular system reacts abnormally in fever is much more precise. It is a quarter of a century since Heidenhain (15) showed that whereas in health the effect of reflex stimulation of the vaso-motor centre is to increase the cutaneous circulation, and thereby bring down the temperature of the blood, this is not the case in fever, but rather the contrary. There is no dilatation of the cutaneous vessels, no increase of the temperature of the extremities — a result which we can best explain by saying that the normal vascular response to stimulation takes place less readily than before; or, in other words, that the nerves and centres which preside over that response are no longer capable of discharging their function efficiently.

The subject is one in respect of which results as valuable can be obtained by clinical investigation as by experiments on animals; for of the three criteria by which the physiologist judges of the quantity of blood contained in a part — its volume, its temperature, and its colour — the first two can be as well observed in man as in animals, and the third better.

The changes of volume of the limbs in fever have been very successfully examined by Dr. Maragliano of Genoa, with the aid of Mosso's plethysmograph. By a preliminary series of experiments it was first ascertained that in healthy persons, after a meal, the volume of the arm, as thus measured for a number of hours, slowly declines as the time which has elapsed since taking food increases, and that the rate of this decline is uniform. The same method of observation was then applied to a variety of typical fevers. In ague it was found that the accession of an attack is marked by a very obvious diminution of volume, which is antecedent to the rigor; and that in the crisis likewise an increase of volume is always the harbinger of the critical thermolysis. The measurements given, however,

seem to show that, in intermittent fever at all events, the interval between the expansion of the arm and the fall of the temperature is much longer than that between the contraction and the rise. In some cases in which the fastigium lasted for some time with a temperature of over 104°, the critical expansion was preceded by a gradual enlargement of the arm which could be observed for hours before there was any change in the readings of the thermometer.

As regards the *temperature of the surface* we possessed until lately very little reliable information. The best clinical observations, so far as I know, are those recently made by Dr. Geigel at Würzburg, by a thermo-electrical method, of which it is sufficient to say that the apparatus consists of a single pair of junctions, one of which can be applied to the skin, the other being in a vessel containing oil at known and constant temperature. Simultaneous measurements were made of the temperature at four different spots — some covered, others exposed — and compared with readings of the temperature in the rectum taken during the same period. The results, which are of special interest in connection with the Genoa observations, may be best stated according to the stage in the febrile process to which they relate. In rigor it was found that the surface temperature sinks very considerably, and consequently that the difference between the surface and internal temperature — the latter rising while the former falls — rapidly augments. On this subject the data given are so unequivocal that the often-repeated statement, that while the patient shivers the skin becomes hotter, can no longer be made. As regards the period of defervescence, it is as clearly shown that the fall of the blood temperature is preceded by rise of surface temperature — that while the internal parts are still at fever heat the temperature of the skin rises — in consequence of the more ample afflux of blood to the surface, the relation between this afflux and the critical sweating being most strikingly shown by the temperature curves. Another interesting point is that in the fastigium, notwithstanding that to the hand the skin feels hot and dry, its temperature is only a little greater than in health — less than that which it attains as defervescence approaches.

We have thus perfect harmony between what has been learnt from the observation of surface temperature and the results of plethysmographic measurement. Increase of volume of the extremity and increase of the temperature of the surface mean the same thing, viz., that the flow of warm blood as supplied through the skin is augmented. It is thus that the organism reacts promptly and effectually against any increase of the temperature of the blood.

4. **Cerebral Heat Centres.** — Although it may be doubted whether the pyrexia, which is produced by stimulation or injury of the brain, comes under the designation of "fever," the facts relating to this subject cannot be passed over in the present discussion. For in some instances the pathological state observed, if not fever, so much resembles it that it cannot fail to be of interest to compare the one with the other. Space will not allow me to refer in any detail to the older observations relating

to the effects of severance of the spinal cord in the cervical region and of injury of the bulb. It is sufficient to say that the observed effects of section of the spinal cord were such as to show that the animals experimented on were incapable of maintaining constancy of temperature, while on other grounds it seemed probable that the antagonistic functions of production and discharge of heat were presided over or regulated by different parts of the intracranial nervous system. Since 1880 the question of the localisation of these functions has assumed a different aspect. In that year Dr. Wood of Philadelphia discovered that injury of a certain part of the cortical motor area which surrounds the crucial sulcus in the dog produced pyrexia. Soon afterwards it was discovered independently in Paris and in Berlin that a thermogenetic region exists on the medial side of the corpus striatum, the excitation of which, whether by puncture or electrical currents, gives rise to a similar increase of temperature. The conditions and results of the experiment were most carefully investigated, under the guidance of Professor Zuntz, by Aronsohn and Sachs (20), who found that the thermogenetic region corresponded in position to the *nodus cursorius* of Nothnagel, and was strictly limited. It was also found that the pyrexia, which did not come on until some time after the injury, was accompanied by an increased elimination of nitrogen, so that at first sight it might appear as if a genuine fever had been produced. There are, however, points of difference by which the one pathological state may be distinguished from the other. The "hyperthermic" state produced by puncture is found to differ from true febrile pyrexia above all in the absence of those vascular conditions of the skin which we have seen to be so characteristic. The bodily temperature rises gradually to a febrile height (105° F. to 106° F.), and then as gradually subsides; but there is no rigor, nor is the subsidence preceded by any vascular dilatation. The vessels, indeed, are so incapable of responding in the normal way to their environment, that if the animal be placed in a warm chamber at 37° C. it becomes hyperpyrexic, yet the ears remain pale as before. These facts seem clearly to indicate that the disorder of vascular innervation due to puncture is of a different kind from that of fever, the regulation of temperature being almost, but as we shall see farther on, not completely in abeyance; whereas in fever the power of guarding against excessive thermogenesis is weakened in much less degree. There being this essential difference between brain pyrexia and that of fever, how are we to account for the fact that in Aronsohn and Sachs' very elaborate investigation there was found to be increase not only of the respiratory exchange, but of the elimination of nitrogen (20). The answer is that although Dr. Ringer's observation (1859), confirmed as it has been, both clinically and experimently — that in the accession of fever increased metabolism precedes rise of temperature — clearly proves that in fever the high temperature is not, as some have thought, the sole cause of the nitrogenous waste, yet the evidence that the latter may have this origin is quite as conclusive. A temperature of over 104°, if it continue, produces tissue waste, however it is itself brought

about. The simplest mode of raising the bodily temperature of an animal without inducing any other disorder consists in subjecting it to a temperature just sufficient to prevent a discharge of heat from its surface. Thus, by placing a dog in a chamber at 37° C. its body temperature may be easily maintained at a point approaching that of fever. The result is to produce both of the effects which follow brain puncture. The increase of the nitrogen elimination lasts for two or three days, and is quite as great as that observed (20) in Aronsohn and Sachs' experiment.

5. **Antipyretics.** — The discovery about fourteen years ago of several bodies which possess the power of reducing temperature in fever, and the investigations of their action by various observers, have contributed very materially to the elucidation of the phenomena of febrile pyrexia. Of these bodies kairin, of which the properties were first made known in 1882 by Professor Filehne (21), acts more promptly than any other. Next to it comes antipyrin, which was discovered two years later, and was also first examined by Filehne (22), and has since held its ground as an antifebrile remedy. I allude to them, not with any reference to their therapeutic value, but because the phenomena of their physiological action are well known, and throw light on the process which they counteract.

In man the effect of kairin, as Filehne expresses it, is to "open all the sluices for the escape of heat from the surface." In animals it is equally prompt. The rate of surface loss, as measured calorimetrically by Dr. Richter (23), exceeds by 25 per cent the previous fever rate, and the normal rate by 75 per cent. As the effect, which is of short duration, passes off the discharge of heat diminishes to a point below the normal.

The same year that these observations were recorded, Dr. R. Gottlieb (24) applied the more exact calorimetrical method of Rubner in observations on antipyrin — with this difference, however, that his investigation related not to artificial fever produced by the introduction of pyrogenetic substances, but to the brain-puncture pyrexia referred to above. The results distinctly prove that in the normal animal the diminution of temperature produced by antipyrin is due entirely to increase of surface loss. Notwithstanding that it has been clearly proved that antipyrin in repeated doses in man is known to diminish the discharge of nitrogen (25), it is clear that the increased metabolism which this implies has nothing to do with the antipyretic action, for the increase of surface loss more than covers the diminution of temperature. In brain pyrexia the increase of surface loss after antipyrin is much greater than in health, and probably greater than in fever, for the previous constriction of the cutaneous vessels is greater. The fall of temperature to which this gives rise is also much greater, but still is not so great as it would be if the whole excess of heat loss were at the expense of the organism. It therefore appears that even in brain pyrexia the power which the organism possesses of compensating loss by increased production is not entirely absent.

That the two antipyretics act primarily by augmenting the surface loss we have even more direct evidence from their effect on the temperature

of the skin and of the volume of the extremities; and we have here the additional advantage that in both of these points we can base our conclusions on observations at the bedside. Maragliano (*loc. cit.*) found that the action of kairin and antipyrin in continued fever as well as in ague can be readily observed by the arm-plethysmograph. It manifests itself by an expansion of the limb which accompanies the diminution of temperature; and in typhoid it can be observed that the passing off of the effect and the return of the pyrexia is attended by a corresponding diminution of the volume of the arm. As regards the temperature of the skin, equally satisfactory results are supplied by Geigel, to whose thermo-electric measurements reference has already been made. It is shown that in all cases in which antipyrin produces its characteristic effect the diminution of central temperature is preceded by increase of surface temperature, clearly indicating that the mode of action of the drug is to diminish the temperature of the blood by increasing the rate at which it flows towards the superficial parts of the body.

It thus appears that increased volume of the extremities, increased temperature of the skin, and increased discharge of heat from the surface (as measured calorimetrically) are the characteristic phenomena of antipyretic action in man and in animals. It need not be pointed out that these phenomena are physiologically correlated. They plainly indicate that antipyretics act on that part of the nervous system which presides over the inhibitory or dilating vascular nerves. The bearing of this fact on the question of the nature of fever lies in this, that they afford clearer evidence than can be obtained otherwise, that the power which the nervous system possesses of regulating the loss of heat at the surface is adequate to bring about changes of bodily temperature as great as those which take place in febrile pyrexia. What they do not prove is that fever is nothing more than a disorder of thermotaxis.

6. Ætiology of Fever. — It is now thirty years since Otto Weber and Billroth investigated the fever which is produced by the introduction of septic material into the circulating blood or into the cellular tissue, and showed in what respect the artificial fever resembled or differed from surgical fever. It was soon afterwards found that the products of acute inflammation give rise to fever under similar conditions. And when, at a later period, it was recognised that these products owe their infective properties to the presence of microphytes (as we then called them), the inference naturally followed that the power of producing fever was also dependent on the presence of those organisms.

At that early period (1872) the methods now familiar to the pathologist of discriminating between different kinds of bacteria were unknown. When some eight years later Dr. Koch taught us how to do this, and thus founded the science or rather technique of bacteriology, it seemed likely that the fever-producing property would turn out to be an endowment of particular species, and that by using pure cultivations it would be possible to induce fever experimentally with much greater certainty than had before been possible. This expectation, whether rightly or wrongly

entertained, has not been realised. There are several species which are phlogogenetic, but none which can be relied upon to produce fever. The one which has lately appeared to answer the purpose best is the bacillus of Rouget (the erysipelas of swine), but others, as for example the bacterium coli communis, and the ordinary chaplet-coccus of acute abscesses, are also available.

The question whether the micro-organisms themselves or their products produce fever is an old one. In 1875 I prepared a substance, which I ventured to call pyrogen, from putrid extract of flesh, by first destroying all bacterial life by the addition of alcohol in sufficient quantities to precipitate most of the proteids it contained, separating the precipitate by filtration, evaporating the clear filtrate, and redissolving in water. This sterile product produced fever, but was deprived of that property by filtration through porcelain, whence I conjectured that the pyrogenic substance was perhaps a body analogous to the unformed ferments or enzymes (26). About the same time, experiments made at Dorpat by pupils of A. Schmidt proved that the obscure constituent of the blood to which he attributes the property of exciting coagulation has also that of producing fever, so that the introduction of any material which either contains fibrin-ferment, or gives rise to its formation in the circulating blood, has the same effect (27). It thus became possible to explain why, when transfusion with lamb's blood was in vogue, the operation, notwithstanding antiseptic precautions, was always followed by fever. I think we may associate with these old observations the discussions which have recently taken place on the production of fever by the injection of extracts of fresh tissues (muscle, liver, thyroid, etc.) (28), which have this in common with transfusion of blood derived from animals into the circulation of man, that in both instances there is disintegration of cells.

As regards ferments, it has been shown that all the commercial enzymes are apt to cause fever when introduced into the circulation or into the cellular tissue, but inasmuch as in certain recent experiments pure enzymes prepared at Heidelberg under Prof. Kühne's direction were found to have no such property, it may probably be assumed that in the others the effect is to be attributed to the albuminous products of digestion of which they largely consist. This seems the more probable when we remember that albumoses derived from very different sources have been found to be actively pyrogenetic, the most striking instance being that of the "deutero-albumose" found by Prof. Kühne to be a constituent of tuberculin. A fever-producing albumose has also been obtained by Prof. Krehl from cultivations of bacterium coli commune (29).

The discovery by Koch of the remarkable way in which the substance just mentioned influences the organism of tuberculous individuals, whether human or animal, stirring up in the neighbourhood of the diseased parts inflammation attended by pyrexia, seems to be calculated to throw considerable light on the genesis of fever — and all the more since it has been discovered, not only that extracts similarly prepared from other micro-organisms have the same action, but that proteids of non-bacterial

origin act in a similar way. For a recent publication of Dr. Matthes (30) seems to show that, in common with the deutero-albumose prepared from tuberculin, the similar product obtained by peptic digestion produces both in man and animals the well-known local and constitutional effects of tuberculin, if tuberculous disease exist, but no reaction whatever in healthy individuals. It has indeed been found possible to obtain a proteid body from the same source, which produces tuberculin effects in smaller dose than those of tuberculin itself.

Several questions present themselves in connection with this subject of which it would be premature to speak at present — such as the relation between the group of proteids and the toxins which appear to play so important a part in the specific infective processes, and the relation between the extraordinary physiological activity of these bodies and their chemical properties.

The fact that severe injuries, such as simple fractures, which are necessarily attended with a certain amount of disintegration of tissue, are known to be followed by febrile reaction (31), sometimes of great intensity, notwithstanding that the reparative process is not in the slightest degree interfered with, and that the integrity of the skin affords a certain guarantee for the exclusion of bacterial contamination (29), seems to confirm the inference of Charrin, from the experiments already referred to on extracts of fresh tissues, that in the bodies of all cells "thermogenic substances" — or rather materials from which they can be generated — are contained. However this may be, it is clear that the property of inducing febrile reaction is by no means confined to substances which depend for their existence on bacteria. Susceptibility to the action of fever-producing substances is not only very different in animals of different species, but depends largely on individual peculiarities, whether natural or acquired. We have already seen how it is increased by the previous existence of certain organic diseases, and it may be added that in experiments on artificial fever a "fresh" animal is usually found to be less susceptible than one which has been previously "fevered."

Conclusion

Although I have endeavoured in the preceding paragraphs to state the leading facts and considerations relating to the origin and characteristic phenomena of fever in such a way as to enable the reader to draw his own inferences, it may, perhaps, be convenient that I should state the views which I am inclined to adopt.

In the concluding paragraph of the essay on fever which I published in 1875, I set against each other two possible alternatives (26). Either fever originates in disorder of the nervous centres, producing pyrexia and as a secondary result disorder of nutrition, *or* it originates in a disorder of protoplasm to which the nervous phenomena are secondary. Although the second of these hypotheses seemed at that time preferable to the first, I did not think that either afforded a sufficient explanation of fever so

long as the problem of the normal relation between temperature and thermogenesis remained unsolved. Since that time considerable progress towards this elucidation has been made. By the labours of Rubner the relations between the heat values of the constituents of food and the production of heat, in animals, has been ascertained with such exactitude as to afford a safe basis for investigating the relations between production and loss in various conditions, while from Professor Zuntz and those who have worked with him we have received very complete information as to the way in which the organism reacts to variations in the temperature of its environment in either direction. The researches of Zuntz show conclusively that the only reflex apparatus for regulating temperature *which is always at work* is that which governs the loss of heat at the surface. At the same time, it is obvious that, when required, the organism can bring the other kind of regulation into play. No one doubts that shivering and the other almost involuntary muscular movements which are occasioned by exposure to cold are in a sense reflex. Even in a vigorous person the effect of the cold bath is to induce a tendency to the performance of such movements, the obvious purpose of which is to augment the production of heat (as can be readily shown if the respiratory exchange be measured), and so to compensate the increase of surface loss. But the reflex of shivering has in it a psychical element; it is associated with the sensation of chill, and may be resisted by a strong effort. When this tendency to shudder is resisted, the excessive intake of oxygen and output of carbon dioxide was no longer observable (as Professor Zuntz found when he made himself the subject of experiment). Yet, notwithstanding the absence of any evidence of increased thermogenesis, the temperature was maintained, so that the augmentation of respiratory exchange was evidently accessory, not essential.

Whether in small animals such as mice, in which the surface loss of heat per unit of body weight must be more than ten times as great as in man, there is anything like a reflex regulation of thermogenesis independent of muscular activity, is a question not yet decided. Dr. Pembrey's researches on the subject do not seem to make it probable; for he finds that the power of regulating the respiratory exchange depends on the development and activity of the neuro-muscular system.

In Dr. Macalister's admirable Goulstonian Lectures on Fever it is suggested that thermogenesis, thermolysis, and thermotaxis must be regarded as three separate functions of the nervous system. It seems at first sight difficult to see how, under conditions tending to bring down the bodily temperature, the cooling of the body can be prevented in any other way than by the direct influence of the nervous system on the production of heat. We have learned from Zuntz's experiments that the exercise of this influence is not essential. The key to the apparent difficulty is to be sought for in the consideration, that in a warm blooded animal of constant temperature the supply of heat is always potentially in excess. It is obvious that in a warm room more heat is produced than is wanted, but not so obvious, though equally true, that

in the cold of winter the body temperature would rise at any moment if surface loss were suspended or annulled. In the two cases the "mechanism" is the same. It, therefore, does not seem necessary to imagine more than one regulating centre *in constant operation* — that which presides over surface loss.

The last question to be discussed is that of the relation between pyrexia from cerebral puncture, and febrile pyrexia.

The question is one of words. If the word fever be understood to mean the reaction of the organism to a fever-producing substance introduced into the circulating blood and conveyed thereby to the parts on which it acts, then the pyrexia of cerebral puncture is not fever. In the present paper the term has been used in this sense only. The study of puncture pyrexia is of great interest in enabling us to determine which of the phenomena of fever are or may be secondary to the rise of temperature, and in what degree they may be attributed to it, but it cannot be admitted that the two processes are identical or even kindred. In nosology difference of cause is a distinction which overrides all others.

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THE GENERAL PATHOLOGY OF NUTRITION

The life of the individual is dependent upon the life of the cells or derivatives of the cells, which together make up the organs and tissues of the body. Every cell possesses the property of taking up from the fluid medium by which it is surrounded the substances which are necessary for its vital activity, and of casting out the waste products.

It was John Hunter who said: "Every individual particle of the animal matter is possessed of life, and the least imaginable part which we can separate is as much alive as the whole."

Owing to differentiation of structure and specialisation of function, certain master tissues (*e.g.* glandular, nervous, and muscular) possess, in addition to their general functions of repair and waste, a special function peculiar to each tissue involving storage of material. The mammary gland before lactation occurs is in a quiescent state; its cells are living and awaiting the natural physiological stimulus which will arouse their special function of elaboration and secretion of milk; but, prior to this, the cells are still the seat of that perpetual circulation of matter termed metabolism, constructive and destructive — activities common to all living protoplasm.

Physiologically, the cells of the body are dependent upon one another and upon the circulating blood which, as it streams slowly through the capillaries, brings into harmonious relation the effects of each and all of their vital activities. This functional harmony between the different tissues is brought about by the blood, and serves to maintain a constant in the chemical composition and temperature of that fluid; the maintenance of this constant is essential to the well-being of all the cells of the body. There is thus an interdependence of all the tissues; if one suffers, all suffer.

The dictum of Virchow, *Omnis cellula e cellulâ*, is a fundamental principle underlying all physiological and pathological problems. The fertilised ovum may be looked upon as the fusion of the essential portion

of the male sperm cell with the female germ cell, and with this process there is a fusion of the properties and attributes of the germinal plasm of the parents. This cell possesses, then, specific properties which distinguish it from every other cell in existence; likewise all the cells which are derived from it by segmentation possess specific vital properties which make them differ from the cells which constitute the tissues and organs of another animal. We may not be able to show by chemical analyses and microscopical examination any differences in the tissues of two individuals; they may seem identical; the distinction, however, appears in the differences of adaptation in the cells of the organism to their environment, individually and collectively. The instability and mobility of the material substance of the cell constitutes its life: no portion of the living body is stable, but new formation and regeneration are continually taking place during life, even after completion of the growing period. Many examples of these processes could be cited, viz., the epithelium lining the alimentary and respiratory tracts which is continually being destroyed and replaced; likewise the epithelium covering the surface of the body, and the never ceasing disintegration and new formation of the blood corpuscles. The mechanism by which cells are enabled to take up nutrient material from the surrounding lymph and to cast out their waste products is unknown to us. It is a specific property of the protoplasm of the cell, controlled in the higher differentiated tissues by nervous impressions which not only (as may be proved in the submaxillary gland) directly control the functional activity of the epithelial cell elements, but also the amount of blood flowing through the gland. In health there is a constant *adaptation of repair to waste*; and, although the organic form of the cell or fibre is generally preserved, the contents are continually undergoing molecular and chemical changes, with conversion of potential into kinetic energy, consumption of oxygen and organic substances, and the liberation of carbonic acid, water, and other waste products. The energy is replaced and the tissue waste repaired by the circulating blood. This, however, necessitates a constant in the quantity, quality and temperature of the blood, which can only be affected by the assimilation of oxygen, food and water in such proportion as to make up that which is lost to the body by disassimilation in the tissues, and elimination by the lungs, skin and kidneys. "A man can live a few minutes without oxygen, a few days without water, and a few weeks without food" (Waller).

The *balance of nutrition* may be maintained when the export is repaired by a corresponding import; and physiologists have shown that the minimum daily income required by a healthy man performing his average daily work, and maintaining his usual body weight, is 5 per cent of that body weight—1 per cent being solid food, 1 per cent oxygen, and 3 per cent water. These amounts may be modified by various circumstances, such as climate, work, age, convalescence from illness, lactation, and the like.

An infant or growing child requires not only food for repair but also for new growth. A mother during lactation, over and above the normal

amount of nourishment, requires a suitable excess to provide the milk necessary for the suckling infant.

If digestion and assimilation are normal the blood will be maintained at a constant in its chemical composition; should there be, however, an insufficiency of the intake, inanition will follow. Inasmuch as the intake of food is *always intermittent,* and owing to exigencies in obtaining it is at times very much so, certain tissues and organs of the body possess *storage functions* which provide reserve material upon which the blood can draw as required. The storage of fat in the connective tissue and liver cells of the body represents so much potential energy. The glycogen in the liver is a store of carbohydrate which is continually being utilised in maintaining an average constant of sugar in the blood. The sugar is used up continually by the muscles in the production of energy, but if more than a certain quantity exist in the blood, it would be injurious; consequently the liver intercepts the intermittent supply of carbohydrate material in the form of glucose absorbed by the portal blood, converts it into glycogen, and stores it in its cells to be used as required (Bernard). Probably all the cells of the body possess the power of oxygen storage; we have definite proof of its existence in the muscles. The muscles of the frog can contract and produce heat and work in an atmosphere of N with liberation of CO_2 and other waste products; and the muscles of warm-blooded animals will display similar functional activity (when stimulated) for some time after the circulation has ceased. During sleep and rest the tissues are storing up materials for their functional activity, and this has been most clearly shown by the histological appearances of the cells of secreting glands during rest and during activity. Another very important factor complementary to destructive metabolism, in connection with the maintenance of the normal composition of the blood, is what is termed the *internal secretion of glands.*

Blood — the Nutrient Fluid and Medium of Exchange. — The quantity of blood in the body is about $\frac{1}{14}$th of the body weight, and its mode of distribution is varied in accordance with the functional needs of the tissues. Certain organs and tissues, requiring large quantities of blood to perform their functions, are highly vascular in proportion; the supply to a part is regulated automatically by the vaso-motor nervous system, and the physiological stimulus which excites the activity of an organ may also determine an increase of blood to the part. Thus, experimentally, an increase of urea in the blood causes an expansion of the kidney due to vaso-dilation, which signifies an increased flow of blood associated with the secretory activity of the organ.

There is an essential similarity between the composition of protoplasm and that of the normal human body — between the normal human body and the circulating blood which provides it with nutrition; for, during gestation in utero, a new body is entirely built up from the maternal blood; and there is also an essential similarity between milk, the natural food of the suckling animal, and the composition of the body — with one important exception to be mentioned hereafter. The cells of the body

assimilate from the blood organic proximate principles representing so much potential energy, which they convert into kinetic energy in the form of mental and bodily work.

Cell activity, then, depends upon chemical action, and the products of cell activity are carbonic acid, water, and nitrogenous waste products, of which urea is by far the most important.

To restore to the blood that which it has given up to the tissues requires daily ingestion of a certain amount of food in the form of organic proximate principles: proteids, carbohydrates, fats, water, salts and oxygen. The proximate principles which enter into the composition of the human body are composed of fourteen elements, united in various combinations to form complex energy-producing organic substances and simpler inorganic substances — the latter incapable of producing energy, but still essential for nutrition, water making up at least two-thirds of the body weight. The elements contained in the body, and therefore in the blood, are C. H. O. N. S. P. Fe. Na. K. Mg. Ca. Cl. F. Si. Although many of these exist in very small quantities, yet in all probability they are essential to the blood for the proper nutrition of the cells of the body. Even fluorine, which exists only in minutest traces, is essential to the formation of the teeth and bones.

"The law of the minimum" holds as good for the nutrition of the human body as it does for agriculture; that is to say, the food must contain not less than certain quantities of the above elements, and in such forms as can be assimilated. Iron is the element of great importance in connection with the function of oxygenation of the tissues, by means of the iron-containing hæmoglobin. The iron in the body of an average-sized man is 3 to 5 grammes, the greater part of which is contained in the blood in the form of hæmoglobin; the rest is combined with nucleo-albumins of the tissues. Bunge points out that the ash of a bitch's milk corresponded with the ash of the body of the puppy in every respect save one — there was six times less iron. The explanation of this doubtless lies in the fact that the young animal acquires its store of iron during its development *in utero*. The proportional amount of iron to the weight of the body is highest at birth, and gradually diminishes with the development of the animal during lactation. These facts may explain the wonderful effect of small doses of iron and cod liver oil on the nutrition of ill-nourished, rickety infants, and the advisability of not deferring weaning or not adhering too long to a purely milk diet, but of using food which supplies more iron.

We obtain in our food enough of all the inorganic salts save one — sodium chloride; but our diet is by no means deficient even in this. No animal can live if its food be deprived of salts. It has been suggested that as the blood loses a large amount of its inorganic salts, and these are not replenished by the food, there are no bases to unite with the $S.O_3$ formed by the oxidation of the sulphur of the disintegrated proteids. It is probable that the salts favour osmotic changes by their power of diffusion; and certain salts, especially sodium chloride, play

an important part in nutritive exchange by holding in solution in the blood and muscle plasma certain proteids of the globulin class. The important part played by lime salts in the formation of bone and by potash salts in the tissues is well known. [*Vide* articles Rickets and Scurvy.]

Proteids are essential to restore to the blood those proteid substances which have been used by the tissues for repairing waste. Muscular energy can be obtained from proteid, but normally it is obtained from carbohydrates and fat, a more economical method. It has been found, however, that proteids alone can repair tissue-waste, and that if proteids are not contained in the food in proper proportion the tissues feed on themselves. In inanition or starvation, on the other hand, a selective process seems to take place, and the tissues which are of the least consequence suffer the most. Fat rapidly disappears, muscle wastes; so also do many of the glands, the spleen, and liver, and even the blood itself; but the circulating medium nourishes the nervous system and heart, so that the master organs essential to the life of the individual may be supported at the expense of the less important tissues. This vicarious nutrition may be considered as a defensive power of the organism to resist dissolution of the nervous system and heart.

Dr. Barlow (in the Bradshaw Lecture, 1894) has shown that condensed milk or even sterilised milk is not an efficient substitute for the natural food of the suckling infant, and that infantile scurvy may be occasioned by their sole use. It is a noteworthy fact that although animals can live on milk alone, yet if a mixture be made of all the supposed constituents of milk which, according to the present teaching of physiology, are necessary for the maintenance of the organism, the animals fed on it rapidly die. Does milk then, besides carbohydrates, fat, proteids, salts and water, contain other substances indispensable to the maintenance of life?

Of like importance in nutrition are certain phosphorus-containing substances in the body, viz., a phosphuretted fat termed *lecithin*, indispensable for the constructive metabolism of the central nervous system and red blood corpuscles; and *nuclein*, which consists of an organic phosphorus-containing acid, termed nucleic acid, in combination with proteid. The amount of P varies in different forms of nuclein, as the sulphur varies in amount in different forms of proteid. Nucleic acid contains C. H. O. N. P but no S. The nucleus of a cell serves two functions — the nutritive and the formative; it exercises a controlling influence on the nutrition of the cell, and it is in the nucleus that the first evidences of cell-proliferation are manifested. The essential portion of the male sperm cell, namely, the head of the spermatozoon, chemically consists entirely of nucleic acid.

The composition of cells is mainly *spongioplasm* and *hyaloplasm*; the former is the meshwork in which the latter more fluid protoplasm is contained. The spongioplasm stains readily, and is therefore called chromatin, a body which contains both P and Fe. Experiments seem

to show that the daily output of uric acid is derived from destructive metabolism of nucleo-albumin. If this represent the total N derived from the waste of nucleo-albumin, it shows how very small is the destruction of the fixed framework of the cell elements, and how carefully are these highly complex organic bodies preserved from waste. The fluid which surrounds and bathes every cell of the body is a transudation from the blood; and it is the property of every anatomical element to take from the fluid the materials which it requires, to incorporate them for a time, to utilise them in various ways according to its special function, and to give back to the fluid various waste products or bye-products, the outcome of its functional activity. There is thus going on in the cells a continual and associated process of *recomposition and decomposition — of constructive and destructive metabolism* — a nutritive exchange essential to all forms of physiological function, whether it be of body or mind.

The deficient supply of blood or deficient quality of the blood is, then, one of the causes of nutritive derangement, and of cell-degradation and death. Another cause may be, *the failure on the part of the organism to eliminate the waste products which accumulate in the blood*, causing injury to the cell elements, as in uræmia.

There is yet another cause of defect of nutrition due to alteration of the blood, which lies in *the interdependence of each and all of the tissues of the body upon one another.* No part can be removed without some effect upon the rest of the body. We may note, for example, the profound effect on nutrition and on the male character produced by early castration; and recently various other organs have been shown to exercise a very considerable influence upon the blood and tissues by acts complementary to their special functional activity. I refer to those **glands** believed to have an **internal secretion** passing into the blood and playing an important part in metabolism; and I shall now consider certain of these functions.

I. *The Liver.*[1] — Minkowski has shown that, after extirpation of the liver in birds, uric acid is in great part replaced by ammonia and lactic acid. It is impossible to extirpate the liver in warm-blooded animals; but Murchison always taught that nitrogenous waste products of tissue-metabolism were converted by the liver into urea. It is known that in acute yellow atrophy leucin and tirosin appear in the urine. There is not the slightest doubt that urea is far less poisonous than its antecedents; moreover, urea favours urinary secretion, and may be considered a physiological diuretic. The experiments of Hahn, Masson, Pawlow, and Nencki have shown that in dogs carbamate of ammonia may be made to accumulate in the urine, that it is highly poisonous, and that it arises from tissue metabolism and disintegration. They also found that the injection of sodic carbamate into the circulation of dogs was poisonous only to those animals in which the portal current had been diverted into the vena cava, the portal vein ligatured, and the liver thus thrown out of action (fistula of Eck). This suggests that the car-

[1] As this is mostly new work the names of the observers will be mentioned in the text.

bamate of ammonia is converted into urea by the liver. When the hepatic artery is simultaneously ligatured there is a great increase of carbamate of ammonia. It has been shown that small quantities of this salt exist in the blood, and animals in which the liver is normal suffer no ill effects from its injection; whereas those in which the liver has been put out of action die of peculiar nervous phenomena. These observers think the intoxication of the organism by the products of cellular activity is a complex process, and that their experiments show that one function of the liver is to destroy and transform poisons arising in the organism from cellular activity. Their long series of experiments indicate that the liver protects the organism from poisoning by the products of its own cellular activity; and they make it probable that certain complications arising in hepatic insufficiency of various kinds are due to carbamate of ammonia. It is probable, however, that this is one only of many nitrogenous antecedents of urea.

The liver, again, standing as a safeguard between the portal and general circulations, protects the body from the influence of toxic substances produced by the alimentary canal or taken into it. The researches of M. Bouchard have proved that, for the same quantity of nitrogen, urea is forty times less poisonous than ammoniacal salts; and in his recent work on *Auto-intoxication* he has demonstrated that this function of the liver diminishes in an enormous proportion the toxicity of the waste products.

II. *The Pancreas.* — Recent researches and clinical observations have shown that this organ, besides its digestive functions, discharges into the blood certain products without which the organism is incapable of utilising the glucose normally contained in the blood; hence this accumulates and gives rise to glycosuria or pancreatic diabetes. Von Mering and Minkowski have proved that animals from which the pancreas has been completely extirpated become glycosuric. Lancereaux and other clinicians had previously called attention to lesions of the pancreas in association with diabetes. But the trouble does not seem to come from the accumulation in the organism of a poisonous substance, for no effect is produced on a healthy dog by injecting into its system the blood of an animal which has become diabetic by extirpation of the pancreas. Gley succeeded in tying all the veins of the pancreas and produced glycosuria; and other experiments seem to show that the pancreas has normally a function of elaborating and turning into the blood a glycolytic ferment, necessary to enable the tissues to utilise the sugar contained in it. Complete extirpation of the pancreas (like complete extirpation of the thyroid) must be attained in order that the sugar may thus accumulate in the blood.

III. *The Thyroid Body.* — As early as 1856 Schiff proved that dogs in which he had completely extirpated the thyroid gland, presented numerous troubles and alterations of nutrition analogous to those observed in man after thyroidectomy. He put forward the hypothesis that the thyroid elaborated a substance which passed into the circulation,

and which played an important role in the nutrition of the nervous system. This has since been verified experimentally and clinically. [*Vide* art. Myxœdema.]

IV. *The Pituitary Body.* — Experiments by Gley have shown that in a rabbit which had survived thyroidectomy, destruction of the hypophysis cerebri would lead to trophic troubles similar to those produced in the dog by total extirpation of the thyroid. [*Vide* article Acromegaly, a peculiar hypertrophy associated with disease of pituitary body.]

V. *The Suprarenal Capsules.* — Addison pointed out a peculiar pigmentation of the skin associated with caseous degeneration of these glands. Brown-Séquard has shown that extirpation caused great disturbances of nutrition, often followed by death. In all cases of ablation of these organs there is accumulation of pigment in the blood, and also, according to the researches of Abelous and Langlois, of poisonous products of unknown nature. Schäfer and Oliver have lately shown that injection of suprarenal extract into the circulation of animals is followed by an enormous rise of blood pressure. They have come to the conclusion that the medullary portion of the gland secretes a material which increases the tone of all muscle tissue especially of the heart and arteries.

Bradford's experiments also show that *the kidneys*, besides the functions of elimination of waste products, possess another concerned with the metabolism of the tissues. [*Vide* art. Gen. Path. Dis. of Kidneys.] *The spleen*, in contradistinction to the above-mentioned organs, can be removed without producing any notable physiological effect beyond compensatory hypertrophy of the lymphatic glands.

Influence of the Nervous System upon Nutrition. — The influence of the mind upon the nutrition of the body is well known: anxiety, mental strain, with associated insomnia, are followed by lowered nutrition and general wasting of the body. Many neuroses — such as hysteria, epilepsy and insanity — are associated with failure of nutrition and general wasting of the body; and this condition also obtains in certain cases of nervous exhaustion in highly intellectual persons. Improvement of the nutrition of the body is often followed by improvement of the mental state, as in mania, melancholia, hysteria and neurasthenia.

The question before us, however, is not whether derangement of the nervous system may prevent assimilation, but whether the nervous system exercises a direct trophic influence upon the tissues? We have undoubted proof within the nervous system that nerve-cells exercise a trophic influence upon nerve-fibres; but are there nerve-fibres which can modify the "nutritive exchanges" of the cells independently of the vascular or other known changes? In reply I shall treat of the experimental data, reserving clinical incidents for the articles Hypertrophy, Atrophy and Necrosis.

Intracranial section of the fifth nerve produces inflammation of the eye, ulceration of the cornea, and suppuration and destruction of the eyeball of the same side; but it is asserted that these accidents do not

occur if the eyelids are sewn together, and the delicate surfaces of the conjunctiva and cornea thus protected from the injury of foreign bodies, especially microbes.[1]

Section of the cervical sympathetic is said to produce in a young rabbit an increased growth of the ear; section of the facial nerve to produce an increase in size of the maxillary bones: doubtless in both cases the results are due to increased vascularity, and consequent increased nutrition of those parts.

Section of the anterior roots or motor nerves offers perhaps the best evidence of trophic influence, for the wasting of the muscles is then much more rapid and extensive than disuse of the muscles would produce; and it is attended by electrical changes with "reaction of degeneration." Some physiologists object that the effects may be due to disuse, irritation, or vascular changes; but in my opinion they are a proof of direct trophic influence, for Professor Sherrington and I have produced complete disuse of the muscles of the limb by section of all the posterior afferent roots of a limb — the anterior motor roots being left intact. Animals kept alive three months had never been seen since the operation to use the hand or foot of the limb thus deprived of sensation, yet on stimulation of the cortical centre or of the nerve presiding over these muscles, a contraction was obtained even more readily than on the sound side. Certainly the assumption of a direct trophic influence of the nervous system upon the cells and tissues of the body helps us to explain many important clinical phenomena; but it cannot be asserted that the clinical facts afford indisputable proof of the existence of independent trophic nerve fibres.

The Acquired or Inherited Specific Properties of the Blood and Tissues. — On the failure of nutrition in wasting diseases such as phthisis, cancer, infectious diseases, the reader is referred to special articles; so also on the effects of poisons such as lead, alcohol and phosphorus.

The "*durability of life*" of the cells of each and all the tissues of the body depends largely upon specific inherited properties of longevity. It may happen that all the organs of the body possess an inherited longevity, that if environment be favourable all the tissues will pass through all the stages of growth and natural decay, terminating in gradual dissolution; and the organism pass out of the world as unconscious of death as of birth. On the other hand, there may be an inherited defect in the "make-up" of one particular tissue, rendering it susceptible to disease and degeneration. Should such a tissue be endowed with an important function which cannot be assumed by another

[1] Professors Goltz and Ewald showed (at the International Physiological Congress held at Berne 1895) a dog in which the spinal cord from the last cervical segment downwards had been removed. The muscles of the bladder and rectum preserved their tonus, and there were no trophic changes in the skin, hair, and nails; but of course all the striped muscles of the lower limbs had completely wasted. Inasmuch as the spinal ganglia and sympathetic ganglia had not been destroyed, it may be inferred that the absence of changes in the skin and appendages depended upon integrity of the former, and the preservation of the smooth muscle fibres of the viscera on the integrity of the latter.

tissue, then the whole of the tissues of the body would suffer either from the effects of mal-assimilation or non-removal of the waste products; and the local disease would then cause a derangement of nutrition of the whole organism and perhaps a general dissolution.

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PROGRESSIVE AND GENERAL FAILURE OF NUTRITION

General arrest of nutrition of the tissues of the body will produce *somatic death*. General wasting or inanition may arise from diseases such as cancer or stricture of the œsophagus; destruction of the mucous membrane of the stomach by corrosive fluids or disease; uncontrollable vomiting and hysterical anorexia; pressure of growths upon the thoracic duct; cancer of the pyloric end of the stomach, and cancer of the pancreas. Whether cancer produces its characteristic cachexia by interfering with digestion and assimilation, or whether some products escape from the growth into the blood, or some substance is taken from the blood by the growth, thus altering its composition, is at present matter of speculation; but certainly the sarcomata, which are of mesoblastic origin, do not produce the same marked effect upon nutrition as carcinomata.

There are a number of diseases which produce general wasting by increased destructive metabolism accompanied by fever, by hæmorrhages, or by exhaustive discharges from the body, in none of which the process of repair is adequate, and a progressive failure of nutrition ensues; such are fevers, phthisis, diabetes, prolonged suppuration, dysentery and albuminuria.

General wasting from exhaustive diseases is always attended by a certain amount of tissue metamorphosis and degeneration, as in coagulation necrosis, hyaline degeneration, fatty degeneration, lardaceous degeneration, etc., — the location of the tissue change depending upon the nature of the disease and the ability of the organ or tissue under

abnormal conditions of nutrition to maintain the equilibrium between repair and waste.

In general wasting of the body from starvation the various tissues are affected unequally: 97 per cent of the fat is lost, 30 per cent of the muscle, 28 per cent of the blood, and of the heart only 2 per cent. Wilks and Moxon point out that in cancer the heart usually wastes very much, in one case being reduced to 4 oz.; whereas in phthisis it does not atrophy, although there may be extreme emaciation of the body. Perhaps in the former it is partly disuse-atrophy, owing to the progressive diminution of the amount of blood and tissue.

In old age there is a gradual wasting of all the tissues of the body (the heart sometimes excepted). There may be a *simple atrophy of cell elements* without structural modification, due to a lowering of the vital activities of all the tissues, or *various degenerative* processes common to senile decay.

Retrogressive Disturbances of Nutrition

A. Necrosis or Tissue Death. — Necrosis of a tissue may be partial or complete. The essential specialised cells of an organ or tissue may die, while the mechanical supporting tissues remain and undergo proliferation. Since the former cannot regenerate, the latter fill up the gap. If tissue death or necrosis occur in situations favourable to the presence or introduction of micro-organisms, then we have no longer an aseptic, but a septic necrosis, or gangrene; of this there are two varieties, moist or spreading, and dry. In the former the conditions are favourable to the growth and spread of the putrefactive microbes, in the latter they are not; hence the process is usually limited by a "line of demarcation."

Causes and Pathogeny

Traumatic. — (1) Mechanical injury, such as violent contusions or tight bandaging. (2) Heat and cold. (3) Chemical, such as strong corrosives, acid or alkaline. (4) Electricity. These causes produce complete death of the tissue as a rule, and are, at any rate at the onset, aseptic.

Mechanical injury produces death of the tissue by inducing blood stasis, and by its direct effect upon the tissue elements.

Heat produces death by coagulation; several very important albuminous substances, *e.g.* myosinogen and fibrinogen are coagulated at 56° C. This would indicate that the tissues and fluids of the body exposed to this temperature would solidify, and thus inevitably be killed. Temperatures below 16°–18° C. destroy living protoplasm; the nature of the tissue and the period of time to which it is exposed to abnormal conditions of temperature will determine whether it can be restored to functional activity.

Corrosive Fluids. — Strong acids produce immediate death by *coagula-*

tion of the blood and tissues. Strong *alkalis* disorganise the tissues by *liquefaction* producing a soft eschar.

Electrolysis. — At the negative pole the eschar is soft and resembles the destruction produced by alkalis, whereas at the positive pole the eschar is dry, yellowish, and similar to the effect produced by acids.

B. **Necrosis by Disturbance of the Circulation.** — All causes which bring about *stasis* of the blood in the capillaries, such as inflammation, pressure, hæmorrhage, or blocking of the venous outflow of a part, will cause necrosis by arrest of nutrition. Again, if the arterial supply of a part be cut off by ligature, embolism, thrombosis, or slow degeneration and obliteration of the vessel, anæmic necrosis results. The arrest of the circulation need not be permanent; it suffices if it persist a certain time. The more highly specialised a tissue the briefer its vitality when deprived of blood. The gray matter of the central nervous system, the epithelium of the intestine and the kidneys, can live but a short time (one to two hours, Cohnheim) without their blood-supply. So if one of the above causes should lead to anæmia of a specialised tissue, death of the specialised cell-elements has generally occurred before the circulation can be re-established. This is particularly liable to happen in organs having terminal arteries. [*Vide* arts. Thrombosis, Acute Perforating Ulcer of Stomach and Duodenum.] Direct injury, if severe, produces tissue-necrosis by complete arrest of nutrition of a part; but those remoter causes which consist in the weak defence of the organism against injury, although subsidiary, are quite as important. Thus comparatively trivial immediate causes may produce a spreading necrosis and circulatory disturbances of nutrition, which in a healthy individual could easily be overcome. The predisposing causes are: —

(*a*) *Disturbances of Innervation.* — We have argued that division of the fifth nerve proves no more than that the loss of innervation of the cornea causes sloughing, by abolishing the reflex defensive mechanism of the tissue against microbes. Section of the posterior roots in monkeys produces sores upon the feet, but section of an equal number of roots supplying the upper limb produces no sores upon the hands; the hand is not subjected to the same direct injurious influences of pressure and microbic infection. Charcot maintained that acute decubitus occurring upon the buttock of the paralysed side in some cases of apoplectic hemiplegia was a proof of the existence of direct trophic influence. He stated that when certain patients had only lain on the non-paralysed side, and every precaution had been taken about the urine and fæces, yet within some hours or days a purplish erythematous rash might appear, and bullæ form and burst, leaving a red, sore surface followed by an eschar and usually by sloughing out of the mortified part. Local infection may then ensue and become general. In acute myelitis the bed-sores occur over the sacrum and heels. Déjérine and Leloir, also Pitres and Vaillard have shown that changes in the peripheral nerves often occur in cases of hemiplegia with acute bed-sores.

Trophic changes occur in Morvan's Disease and syringomyelia; of

the former painless whitlows are an essential feature. The perforating ulcer of locomotor ataxy is another example of tissue-necrosis due to changes in the peripheral sensory nerves. Herpes has been observed as a complication of gangrene. Whatever view be taken of the existence of trophic nerves, the important fact remains that disturbances of the normal nervous influences, vaso-motor and sensory, of the skin directly modify the nutrition of the parts, and interfere with the defensive action of the organism against microbic invasion.

Raynaud's Disease is a local asphyxia which is often followed by symmetrical dry gangrene of the extremities. The observer after whom the disease is named considered it to be due to constriction of the small arteries owing to vaso-motor spasm. A number of cases, however, have been brought forward showing endarteritis obliterans. [*Vide* art. Raynaud's Disease.] It is possible also that acute perforating ulcer of the stomach may be induced by reflex vaso-motor spasm.

(*b*) *Lowered Vitality of the Tissues.* — Age is relative; the vital reaction of cells is partially dependent upon inherited specific properties and partially upon present conditions of nutrition. Premature decay of tissue may be inherited or acquired, and death ensues as soon as the vital energy is unable to cope with the antagonistic influences of its environment. Senile decay and death, however, come sooner or later to the healthiest tissues in the most favourable surroundings; it comes when the original vital capacity is exhausted, when the mainspring of life is worn out. Whether then the lowered vitality of the tissues be premature or natural, the tendency to necrosis and gangrene is much greater when an immediate cause exists, such as direct injury or disturbance of nutrition. Many diseases are specially liable to be followed by gangrene and bed-sores. Gangrene of the scrotum, penis, and even of the nose, has been known to occur in cholera (Fagge). In typhoid fever, Liebermeister points out that gangrene and necrosis of bone may occur; chancres may lead to spreading gangrene, and gonorrhœa to sloughing of the penis. Bed-sores are very apt to arise even during convalescence. During and following typhus fever gangrene is not infrequent, and noma of the cheek and vulva is not uncommon after measles. Gangrenous dermatitis occasionally occurs in ill-nourished, tuberculous or syphilitic children. [*Vide* arts. Varicella, Vaccinia.] All these consequences are due to lowered vital resistance engendered by the disease, to lowered defence of the tissues against microbic infection and multiplication, so that microbes gaining entrance to the tissue find a suitable soil for development.

Gangrene of the Lung [*vide* art. Lung]; *Gangrene of Extremities* [*vide* Diabetes]. See also *Phagadæna Tropica.*

The entrance of certain poisons into the blood — *e.g.* ergot of rye, anthrax, snake poison, plague micro-organisms — is followed by necrosis. With regard to ergot it has been supposed that this is due to constriction of the small arterioles by the poison; but instead of the arterial pressure being increased, it is diminished. No doubt many factors are

at work in the gangrene of ergotism. Acute necrosis of the jaw in phosphorus poisoning may also be mentioned.

Secondary Gangrenes. — The presence of gangrene in one part of the body may be followed by *secondary foci* elsewhere. They generally appear in the lung conveyed by an embolic process. It is obvious that the parts most open to infection by the microbes present in the environment are most liable to a gangrenous inflammation. Therefore gangrene especially occurs when the parts affected are in relation to the alimentary canal, the respiratory tract, and the external skin. It only occurs in the nervous system in cases where profound infective ulceration has penetrated the dura mater. It hardly ever occurs in the liver, spleen, kidneys or bones: it generally spreads, but its progress may be arrested by antiseptics and the actual cautery. Eschars produced by physical or chemical agents in healthy people do not spread, as a rule, because the tissues are destroyed or form an unsuitable soil for the development of micro-organisms.

Morbid Anatomy and Pathology of the Different Forms of Necrosis

1. Coagulation Necrosis. — Weigert has shown that when a part of the body rich in protoplasm dies, it usually undergoes coagulation necrosis. In order that coagulation may take place a coagulable material must be present. In all parenchymatous tissues, except the brain, the intercellular fluid is coagulable lymph. When cells die from arrest of nutrition, as in embolism and thrombosis, the first evidence of death is a change in the appearance of the nucleus and chromatic substance: when the organ has been washed free from blood by normal saline solution there are practically no naked eye appearances of a recent infarct; but examined microscopically it is found that the cells or cellular structures do not stain with hæmatoxylon, and that the nuclei have either altered in appearance or disappeared. Halliburton has shown that he can prepare from many tissues a nucleo-albuminous substance, which rapidly brings about coagulation of blood or lymph. The cells deprived of nutrition die, liberating a nucleo-albuminous material, and this reacting upon the coagulable lymph that has penetrated from without, produces a coagulation within the cell. Cohnheim, who gave the name of coagulation necrosis to this necrotic change, considered it to be due to the interaction of the fibrino-plastin and fibrinogen. The process of arrest of nutrition must not be too protracted, or degenerative processes, such as *fatty change*, may ensue and render the process of coagulation impossible. The protoplasm of the cells which have undergone coagulation necrosis somewhat resembles coagulated fibrin in appearance. Often small, transparent, hyaline masses are seen, and sometimes the cells have a homogeneous appearance. The nucleus may be indistinct, absent, swollen up, finely granular, or confused with the contents of the cell. Later the products of

necrosis disintegrate and are absorbed. According to Weigert, these appearances are found in white infarcts, atheroma, caseous degeneration of tumours and glands, waxy degeneration of muscle, and the superficial necrosis of the tissues in diphtheria.

Waxy degeneration of muscle (Zenker) is an example of coagulation necrosis. After death muscle fibre invariably coagulates, but preserves its striation. Under various pathological conditions, such as continued fever, certain muscles (*e.g.* rectus abdominis) undergo a peculiar change. To the naked eye the fibres appear dull and semi-opaque; microscopically they are found to have lost their striated appearance, the contents of the sarcolemma are broken up into lustrous homogeneous lumps, and between the fibres there is a proliferation of the connective tissue cells.

2. **Colliquative Necrosis.** — Sometimes the dead tissue elements are infiltrated with a serous effusion, and then undergo liquefaction. In a burn the cells are killed by the action of the heat, and with them the ferment that would produce coagulation of the transudation of the blood. The dead cells absorb the fluid and swell up, forming a vesicle; or, if the blood be coagulated in the vessels, non-coagulable serum will escape and produce liquefaction of the tissues. Colliquation may follow upon coagulation. In croupous pneumonia the liquefaction of the coagulated products is probably owing to the action of organised ferments. Thrombi also break down and liquefy. In the brain colliquative necrosis occurs as the result of vascular occlusion; the tissues undergo softening and are rapidly destroyed. The cerebro-spinal fluid, which probably represents the lymph of the central nervous system, is a non-coagulable fluid. Hence liquefaction instead of coagulation of the tissues results, and the final part of the process may be the formation of a cyst or cicatrix.

3. **Fat Necrosis.** — Balzer first described this condition in the pancreas and surrounding mesentery. Fitz has shown that it is connected with acute pancreatitis. Whether it be due to a change produced by the steapsin on the fat and to the extension of inflammation from the pancreas, or, as Rolleston suggests, trophic in origin and due to disturbance of the abdominal sympathetic, is not decided; but I am of opinion, from two cases which I have recently seen of acute pancreatitis with fat necrosis, that the process is due to infective micro-organisms.

4. **Caseation** or **Tyrosis** is a mode of termination of necrosis.

5. **Gangrene** or **Septic Necrosis**, of whatever form, is preceded or accompanied by abnormal sensations in the part. It may be coldness or a dull aching, not infrequently severely lancinating or burning. When the integument is involved the pain is more intense, and when an internal organ is affected it may be absent.

Varieties of Gangrene. — Dry — or mummification. Spontaneous gangrene is very liable to occur in old people with atheromatous or calcified arteries. It is limited in extent and chronic in progress. Several causes usually combine to bring about the morbid process: of these are enfeebled

circulation, due to cardiac failure in a remote and dependent part of the body, as the toes or foot, rarely the fingers; and the diseased condition of the arterial wall, by which a gradually extending thrombosis is favoured. The thrombus may extend as far as the popliteal artery, and yet the gangrene be limited to the toes or a portion of the foot. Stasis in the arteries and capillaries of the part, due to feebleness of propulsion, produces the gangrene; and this stasis may be determined by slight injury or abrasion, the cutting of a corn, or any such cause of local inflammation. Putrefactive organisms may be present in the skin, but they require moisture to develop in the tissues: this they do not get, because it evaporates from the surface, especially when the skin separates and peels off. As putrefaction cannot take place there is little or no odour in this form of gangrene. Frost-bite and ergotism lead to mummification, and a physiological example of the process is the necrosis of the umbilical cord. The affected part is generally livid, owing to the contained blood, and the changes in colour are due to its alteration: it becomes withered, black and dry because no more fluid reaches the part, and the remainder evaporates. An inflammatory zone — the line of demarcation — separates the dead part from the healthy. Occasionally dry gangrene may go on to *moist gangrene;* the latter is a necrosis accompanied by putrefaction, and is especially apt to occur in situations which are in direct or in indirect communication with the air, *e.g.* in the lungs, the alimentary canal or the integuments. When septic micro-organisms reach a necrotic part rich in blood, or other fluid, decomposition rapidly sets in, and changes occur in the colour of the part, which assumes a bluish, livid appearance; the epidermis is frequently raised into bullæ and blebs, and a very foul odour arises, due to the formation of various gases which sometimes produce emphysema.

One form of gangrene, *the acute spreading*, is due to a specific micro-organism. The tissues undergo destruction unequally: the blood and softer tissues are first broken up; and, if examined microscopically, broken up blood corpuscles are found, colouring the part, and undergoing transformation into granular pigmentary derivatives of hæmoglobin. The cell-nuclei disappear, and the protoplasm is turbid and breaking up into granules. Muscle fibres lose their striation, and the sarcolemma contains only fatty and granular matters. The connective tissue fibres, owing to the swelling up of the interfibrillary substance, break up into their primitive fibrillæ.

Nerves, owing to their fibrous tissue sheaths, resist dissolution much longer than muscles; but the nerve fibres themselves at a very early period undergo changes in the myelin sheath similar to degeneration. Among the chemical products of decomposition are large quantities of fat which arise even in tissues where there is no fat, such as the lung. Fatty acids — caproic, caprylic, butyric, valerianic — are formed to which, and to ammonium sulphide and hydrogen sulphide, the foul odour is in great measure due. Microscopic examination of the dirty gray, grayish black, or yellowish gray semi-fluid mass into which the tissues

are eventually changed, might show crystals of tirosin, leucin balls, characteristic needles of margarine, and triple phosphates with granules of black or brown pigment. Virchow has shown that a rosy colour can be obtained by the action of nitric acid upon a gangrenous part — the "erythro-proteid reaction." Unless surgery intervene, the powers of the individual to cope with moist gangrene are insufficient; the organisms are diffused by the lymphatics, and finding a suitable soil with warmth and moisture, they grow more rapidly than they can be destroyed by the phagocytes.

Impaired Nutrition.[1] — It has been shown that permanent arrest of nutrition causes cessation of function and death of a tissue. We have now to consider those morbid processes in which impairment of nutrition and a proportional diminution of function ensues. "A cell is not nourished, but nourishes itself." Tissues will, therefore, undergo **atrophy** or **degeneration** when their component cells are unable to maintain equilibrium between repair and waste. The main factors of impaired nutrition of tissues are —

1. *Absence or recession of the normal physiological stimulus.*
2. *Inherent defect of the cell elements to nourish themselves, therefore premature decay.*
3. *Deficiency in the quality or quantity of the blood and lymph supply.*

Any of these factors, singly or combined, may lead to a rapid or gradual retrogressive change of the tissue elements terminating in atrophy and degeneration (both stages towards death); and in some cases the nutritional changes are so extreme that death of the tissue elements does occur. Morbid retrogressive nutritional changes occurring in the master tissues — glandular, muscular, or nervous — and in the vessels, must of necessity be progressive and cumulative, and sooner or later lead to somatic death.

Several abnormal products may arise in the tissues as the result of impaired nutrition. These substances may originate within the cell elements of the tissue from the destructive metabolism of its protoplasm, or be brought by the blood and deposited in the tissue; thus the processes of degeneration are divided into two groups — *metamorphoses*, or degenerations proper, and *infiltrations*. The two conditions are often associated, and to draw a hard and fast line between them is difficult.

The **metamorphoses** are fatty, mucoid, colloid, and lardaceous or amyloid. The normal metabolism of the cell is altered, resulting in chemical and histological changes of its protoplasm, and the metamorphosis may continue until the cell is entirely destroyed. In the earlier stages function is impaired, and in the later stages it may be completely arrested.

The **infiltrations** are fatty, calcareous, and pigmentary; the new material is not a product of the cell protoplasm, but a deposition from

[1] For the effect upon nutrition of inflammatory processes, *vide* article "Inflammation"; in which also atrophic processes arising from inflammatory action are dealt with.

the blood. Since the change is not usually accompanied by destruction of the histological elements, the structure and function of the tissues are much less altered than in the metamorphoses.

ATROPHY AND FIBROSIS. — The various examples of arrested development — such as microcephaly, anencephaly, amyelia, and congenital malformations — are not, properly speaking, atrophic processes due to impaired nutrition, but rather to an inherited developmental defect; so that to them the term *Agenesis* is more appropriate. The peculiar condition termed by Virchow *Hypoplasia* or *Aplasia*, observed frequently in chlorotic girls, is associated with imperfect development of the aorta and larger arteries, accompanied by a remarkable degree of elasticity. The heart is frequently dilated and the left ventricle hypertrophied. These cardio-vascular conditions are associated with imperfect development of the uterus and genital organs.

Atrophy from absence or recession of the normal physiological stimulus. — There are many examples of physiological *disuse atrophies*, *e.g.* of the ductus arteriosus, the ductus venosus, the thymus gland, and the involution of the gravid uterus after parturition. Nutrition and functional activity are interdependent, the two falling off together. The muscles and glands offer excellent examples of tissues which undergo atrophy from disuse; and bones likewise which no longer subserve the statical purposes of the organism — a familiar example of which is the wasting of the alveolar portion of toothless jaws. An example of disuse atrophy in the viscera is afforded after left lumbar colotomy by the dwindling of the large bowel to a scarcely pervious cord.

Cohnheim states — "Nor is it all important whether the failure of a muscle to contract or of a gland to secrete be caused by defective innervation or by occlusion of its duct." He attributes the greatest share in the atrophy to the abeyance of functions. No doubt the falling off in volume of the thigh muscles which occurs in ankylosis of the knee-joint is very great, but experiments upon animals made by Dr. Sherrington[1] and myself lead us to believe that the atrophy of the muscles and reaction of degeneration which occur in infantile paralysis are something more than the effect of disuse; and that the muscles depend for their nutrition upon a physiological stimulus which is continually passing from the anterior horn cells of the spinal cord by the anterior roots and motor fibres of the muscles. If the posterior roots of the lumbo-sacral plexus, or of the cervico-brachial plexus, be divided proximal to the ganglion, the apæsthetic limb is not moved by the animal (even after the lapse of months), there is loss of tonus in the muscle, and a disuse atrophy, yet apparently no degeneration occurs; the muscles can still be made to contract by stimulation of appropriate regions of the cortex cerebri, or of the nerves going to the muscles, as readily, if not more so, than on the uninjured side. If the anterior roots had been divided the

[1] "Experiments upon the influence of sensory nerves upon movement and nutrition of the limbs," *Proceedings of the Royal Society*, vol. lvii., by F. W. Mott, M.D., and C. S. Sherrington, M.D., F.R.S.

muscles would have degenerated more rapidly, and no such results from stimulation could have been obtained. The atrophic effects are still more marked if *both* anterior and posterior roots are divided.

It is necessary to mention a few examples of *correlative atrophy* due to absence or recession of the normal physiological stimulus after amputation of limbs, especially when this has occurred in utero. Atrophy of the tracts and centres in the spinal cord and brain, which are concerned with the innervation of the part, may occur. Thus there is atrophy of the posterior column of the same side and of the antero-lateral of the opposite, and of that portion of the cortex cerebri which is normally concerned in voluntary movements of the limb. Atrophy of the frontal lobe of the left hemisphere has been found associated with atrophy of the opposite lateral lobe of the cerebellum. Atrophy of the fillet and the posterior column nuclei has resulted from porencephalon of the central convolution of the cortex cerebri.

Atrophy of structures which undergo premature decay owing to *inherent* defect of the cell elements adequately to nourish themselves. — Reference to the articles on "Primary Progressive Myopathic (Pseudo-hypertrophic) Paralysis," and to "Friedreich's Disease," will show that the only etiological factor which has been definitely shown to have a causal relation to atrophy of muscle and nervous elements in these diseases respectively is heredity. Facial hemiatrophy and scleroderma from their distribution would suggest a tropho-neurosis, although some authorities consider the condition as a primary wasting of the connective tissue structures for which no reason is known.

It is probable that inherent defect of the cells to nourish themselves is the determining cause of atrophy and degeneration, when the nutrient supply of the tissue is deficient in quantity or altered in quality. These two factors co-exist, and may occasion a general atrophic or degenerative process in one or more of the master tissues of the body.

When glandular, muscular, or nervous tissues begin to undergo nutritional change and decay, the effects become progressive and cumulative in proportion to the functional importance of the organ or tissue to the general nutrition of the body: for this reason in death from disease we seldom find the morbid change limited to one organ.

In all those chronic degenerative affections of tissues occasioned by such extrinsic causes as alcohol, accumulation of nitrogenous waste products in the blood, syphilis, and other toxic agencies (*e.g.* lead, etc.), the degenerative process may commence simultaneously in a number of different tissue elements — glandular, muscular, nervous and cardio-vascular: as we have less reason to believe that the above-mentioned extrinsic factors vary than the intrinsic, we must look to other causes for determining the seat in which the toxic agent will primarily produce the atrophy and decay. These causes may be found in the occupation and habits of the individual.[1] Given *stress* upon an organ or tissue, plus

[1] Edinger has lately pointed out the importance of the occupation and habits of the individual in determining the primary seat of the degenerations of the nervous system,

defective quality and quantity of nutrient supply, degeneration ensues. When, therefore, owing to changes in the blood and changes in the cardio-vascular system, waste is in excess of repair, atrophy and degeneration must occur.

Hereditary factors play a very important part in determining the primary seat of decay; and experience teaches that the more these factors enter into the equation of life, the more the value of x (the life of the individual) proportionately sinks; by no art of the physician can they be removed or modified. On the other hand, toxins can be counteracted by antitoxins, and injurious occupations and habits can be modified or abandoned. Rarely does one of these etiological factors act alone; as rarely are degeneration and atrophy found limited to a single organ or tissue, and the present discussion among pathologists whether atrophy of nervous, glandular or muscular elements be primary or be secondary to the fibrous and vascular change, is of value in showing that the older pathologists were wrong in assuming that the associated fibrous and vascular changes are in all cases the primary cause of the atrophy; it is probably as erroneous to assume that the converse is invariably the order.

As inflammatory stasis, thrombosis and embolism may cause necrosis, so may chronic degenerative changes in the cardio-vascular system be the primary factor in many instances of impaired nutrition and decay; although here again we are met by the argument that arterio-sclerosis is itself a primary degenerative process, and the associated inflammatory changes secondary. Cirrhosis of the liver is usually cited as an example of an organ which undergoes a primary irritative hyperplasia of the fixed connective tissue elements, by the cicatrisation of which the epithelial cells are gradually strangled and undergo atrophy from default of nutrition. Even in the hypertrophied stage, however, degenerative changes may have begun in the liver cells, and this is likely enough, seeing that they are only separated by delicate capillary walls from the blood containing the toxic agent. It must, however, be conceded that the liver cells depend upon the portal blood (which contains the toxic agent) for their functional activity, and upon the blood of the hepatic artery for nutrition. The liver is accordingly a debateable ground of these rival views. I am in favour of the view that the greater proportion of atrophic degenerative processes are due to primary retrogressive nutritional changes of the specialised cell elements. The more highly specialised in function an organ or a tissue the larger the

more especially in tabes and neuritis. He instances the frequency of ataxy in occupations involving much standing; as in officers, railway officials, etc. The relations of overwork of the brain to the production of general paralysis has often been asserted. Amyotrophic lateral sclerosis very frequently commences in the legs, but recently I have investigated two cases in which, apparently, occupation determined the seat of the initial symptons in the hand and arm of the right side. One patient was a cooper who wielded all day long a 4-lb. hammer; the other a woman who earned her living by sewing. It is usually the right hand which is first affected in lead palsy with wrist drop. I have lately emphasised the importance of rest in preventing a localised paralysis in diphtheria from becoming generalised. — *Vide International Journal of Clinics*, 1895.

supply of nutriment, and the more likely are tissues of great physiological activity to undergo degeneration. The cell elements of special function, when destroyed, are unable to regenerate, and repair by fibrous tissue takes place. This is particularly well shown in the central nervous system. Systemic sclerosis of a small but defined tract of the spinal cord or brain can be produced experimentally by cutting off the fibre of an afferent or efferent tract from the cells of which these fibres are but outgrowths — *e.g.* ablation of the thumb area of the cortex cerebri of the monkey produces atrophy of a definite number of fibres of the opposite pyramidal tract, which is followed by a corresponding sclerosis extending only as far as did the degenerated fibres, viz., to the second dorsal segment of the cord. Section of posterior roots proximal to the ganglion is followed, in uncomplicated cases, by degeneration and subsequent sclerosis of the posterior column of the same side. The area of fibrosis is limited to the defined area which may be microscopic, and has absolutely no tendency to spread: it is an attempt at repair; the useless waste products of degeneration are removed by phagocytes, and fibrous tissue fills up the gap. Many authors now believe that the primary systemic degenerative processes of the central nervous system — such as locomotor ataxy, general paralysis of the insane, lateral sclerosis, amyotrophic lateral sclerosis, progressive muscular atrophy, and the sclerosis met with in pellagra, pernicious anæmia and ergotism — are caused by nutritional changes in the ganglion cells of the spinal ganglia, spinal cord and brain. Golgi[1] has shown that every nerve cell possesses one process, the "neuron," which becomes the axis cylinder process of a nerve; and a number of protoplasmic processes, or dendrons, which serve a nutritive function by absorbing the necessary products from the lymph space in which they lie.

Degenerative changes of the cell are manifested by alterations in the number and complexity of the "dendrons," and, in the neuron, by a reversion to the embryonic character and type, followed by degeneration commencing in its terminals and collaterals.

Atrophic Degeneration of Afferent Tracts of the Central Nervous System. — Tabes dorsalis is the best example, and there is much to support the theory of Marie, that the primary change is a nutritional defect of the ganglion cells on the posterior root. In this disease the afferent fibres of the peripheral and central nervous system suffer, which suggests impaired nutrition of the ganglion cells, the outgrowths of which form the sensory tracts. In alcoholic neuritis both motor and sensory fibres suffer; and if we explain the changes of the peripheral nerves in locomotor ataxy by chronic inflammatory changes, why do the motor fibres which are bound up with the sensory escape? why, if it

[1] According to Ramon y Cajal and Lenhossek, the dendrites play the part of conductors the same as the axis cylinder process. The dendrites are, however, receptive in function, whereas the axis cylinder processes are cellulifugal, and if the dendrites do represent agents of nutrition, they would only act by increasing the surface of absorption of the cell to which they belong.

be due to a primary vascular change in the spinal cord, should it be confined to definite tracts of the posterior column? It is more probable that the etiological factor syphilis and the inherited want of durability of the sensory nerve cells determine the seat of this morbid change.

Atrophic Degeneration of Efferent Tracts of the Nervous System. — Progressive muscular atrophy, Idiopathic (?) lateral sclerosis, Amyotrophic lateral sclerosis are all diseases affecting efferent tracts, and the primary change is impaired nutrition, degeneration, and atrophy of one or both of two sets of ganglion cells and of their outgrowths, viz.: —

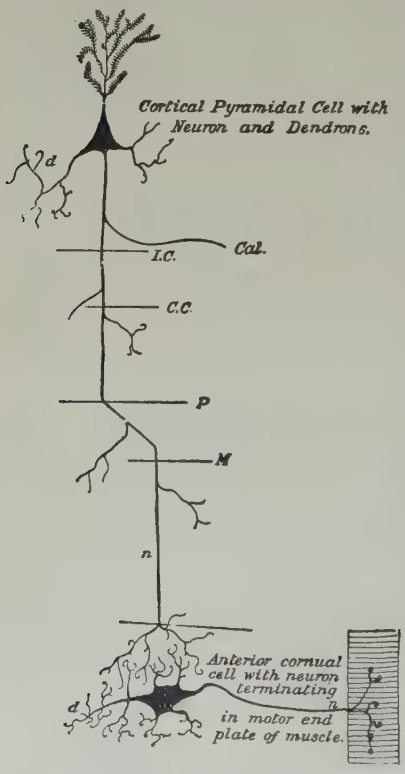
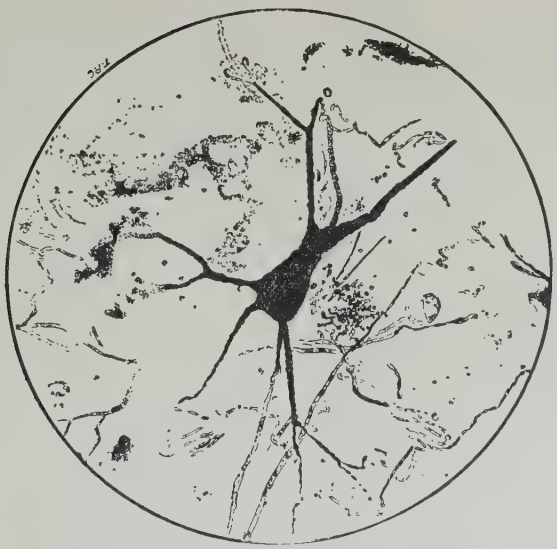


FIG. 5. — Diagrammatic representation of Cortical Pyramidal Cell, with *n*, neuron, and *d*, dendrons representing the *upper segment* of the voluntary motor-path; *Col.*, collateral passing to corpus callosum. Neuron passing through, *I. C*, internal capsule; *C. C*, crus cerebri; *P*, pons; *M*, medulla, where decussation occurs. The neuron is seen to give off collaterals in its course, and to terminate in a fine brush-work of collaterals around the dendrons of the anterior cornual cell.

1. The large multipolar cells of the anterior horns of the spinal cord and their axis cylinder processes which form the motor nerves.

2. The large pyramidal cells of the central convolutions of the cortex cerebri and their axis cylinder processes which form the pyramidal fibres of the spinal cord.

If the lower segment of the motor path be affected the muscles also undergo progressive atrophy. In most cases of progressive muscular atrophy the nutritional degradation of the spinal nerve cell is primary, and the pyramidal tract changes are secondary. In amyotrophic lateral sclerosis the two processes coexist: they are, however, pathologically one and the same. The degeneration of the pyramidal tracts in amyotrophic lateral sclerosis can only be explained by supposing that the disease is a primary impairment of nutrition of the ganglion cells. Cases have been recorded in which all the symptoms of lateral sclerosis — exaggerated, superficial, and deep reflexes — occurred, and yet no sclerosis of the pyramidal tracts; probably only the collaterals, in which the axis cylinder processes terminate, were degenerated, and thus the physiological connection between the cortical centres and the spinal centres was interrupted. (*a*) Cases have been observed in which the degeneration could only be traced (Fig. 5) as



FIGS. 6 and 7. — Microphotographs of two Pyramidal Cells from a case of General Paralysis of the Insane, magnified 400 diameters. The specimen is stained by the Golgi quick method, and the two cells were found in the same section at no great distance from one another. Fig. 6 represents a large Pyramidal Cell with its branching *dendrons* in a fairly healthy condition; these are connected with *mossy-looking* glia cells (or rather lymph spaces surrounding cells), which are seated upon a perivascular lymphatic. According to Cajal, these cells may act as *local vaso-dilators* by contraction of their pseudopodia. From the middle of the base of the cell is seen a *neuron* giving off a *collateral*. Fig. 7 is a large Pyramidal Cell undergoing atrophic degeneration.

far as the medulla, (*b*) in others as far as the pons, (*c*) in others as far as the crus cerebri, (*d*) in others whither the fibres of the internal capsule were atrophied and the cortical cells had in part disappeared or atrophied.

These facts become intelligible if we suppose that the most remote parts of the cell will be the first to suffer from impaired nutrition.

General paralysis of the insane is probably a similar pathological process to tabes and amyotrophic sclerosis, but one affecting also the higher centres of the brain. The periencephalitis by many authorities, however, is considered as primary [*vide* article "General Paralysis"].

Atrophy of the cell elements of glands, as of the *kidney*, may be due to defective blood-supply consequent on change in the arterial walls; the very conditions which are said to give rise to changes in the arterial walls may likewise cause degenerative change of the epithelial elements: yet in those cases in which the kidney is not much shrunken, but in which the arterial changes are great, the primary degeneration is probably in the arteries, *e.g.* syphilitic renal disease. In the granular contracted kidney the opinion that the primary change is a fibrosis, causing atrophy of the epithelium of the uriniferous tubules, is being given up in favour of the inference that a retrograde nutritive change with secondary fibrosis occurs.

Atrophic Changes of Muscle. — In the *heart* fibrous tissue is frequently found replacing muscular tissue; and this condition is termed *fibroid heart*, as if the fibrous tissue overgrowth were the morbid change that produced the atrophy of the muscular fibres. On the contrary, most of such cases are primary degenerative atrophy of the muscular fibre owing to impaired nutrition. When a branch of the coronary artery is blocked by thrombosis or embolism, coagulation necrosis of muscular fibres takes place, and myomalacia results. Although insufficient for the specialised elements, the nutrient supply of the fibrous tissue is unaffected; it receives in fact excess of nutriment, and undergoes a compensatory hyperplasia, which really amounts to a process of repair, and should be considered as a healing process as much as the fibrous tissue formation which unites the two parts of a severed muscle. Perhaps the best example of primary atrophy of muscle with secondary fibrous overgrowth of connective tissue and fat is afforded by Duchenne's paralysis, in which pseudo-hypertrophy occurs. Erb's paralysis is the same disease in the atrophic form; in it there is no overgrowth of fibrous tissue, but atrophy of the muscle only, — a clear proof that the muscular atrophy in the former is not consecutive to the fibrous overgrowth.

Looking upon tissues as composed of living protoplasmic units specialised and non-specialised in function — the former endowed with high metabolic activities, the latter with low — nearly all the nutriment which goes to healthy gland, muscle or nervous matter, is utilised by the special cell elements. Where fibrous connective tissue exists alone the blood-supply is extremely small and the metabolic exchange trifling;

consequently the connective tissue of an organ with a large vascular supply would, by receiving excess of nutriment, undergo hyperplasia (*vide* Hypertrophy) if the specialised element were unable to utilise that nutriment. Thus coexistent with atrophy of one there is hypertrophy of the other; the latter resulting from the former, and not the converse. For the microscopical changes observed in these organs and tissues the reader is referred to the special articles. Pulmonary emphysema may be mentioned as an example of atrophy of blood-vessels and interalveolar connective tissue (particularly the elastic); but this is always associated with changes in the epithelium, and generally with degenerative conditions in other organs.

Mechanical Congestion is by some authors regarded as a cause of atrophy of the specialised cell elements by undue *pressure*, *e.g.* cyanotic atrophy of the liver in prolonged mitral disease.

Fatty Infiltration, *vide* article "Obesity."

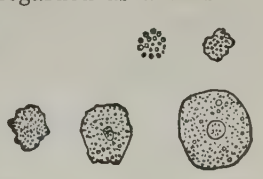


Fig. 8. — Atrophic Liver Cells from Cyanotic Atrophy of the Liver in different stages of degeneration (× 400 diameters). — *Hamilton.*

FATTY METAMORPHOSIS. — Fatty degeneration is one of the most frequent and most important of the pathological conditions associated with lowering of function and destruction of cell protoplasm. It is of especial interest to the physician, as it often affects vital organs and tissues, and is the cause of death in many diseases and in certain forms of poisoning.

Fatty metamorphosis of the cell protoplasm may be a physiological process — as when the uterus undergoes involution after parturition; or the cells of the ruptured Graafian follicle undergo fatty degeneration, forming the corpus luteum; or the central cells of the acini of the mammary glands form colostrum corpuscles. The above-mentioned instances of fatty degeneration show that rapidly proliferating cells will undergo retrogressive nutritional change unless supplied with a proportionate supply of nutriment. The uterus undergoes this retrogressive metamorphosis because the fœtus — the physiological stimulus which determines the increased flow of blood to the organ — has been expelled. The central cells of the mammary acinus undergo fatty degeneration because the peripheral cells require and take all the nutriment. For the same reason, probably, fatty degeneration occurs in the centre of new growths, especially when they are of rapid formation.

It is probable that the cells, thus deprived of adequate nutriment, behave like the starving animal, and liberate vital energy by using up their own protoplasm. In the starving animal, however, there is no deposition of fat granules in the cell, but atrophy only. If, however, a poison, such as phosphorus or CO, be administered to starving animals, then the urea eliminated is increased and fat is formed. Both these poisons interfere, as we shall see, with oxidation processes; the former by a process not satisfactorily explained, the latter by turning out the oxygen from its combination with hæmoglobin. The fat which accumu-

lates in muscle fibres undergoing fatty degeneration is formed for the most part out of organ proteid by the splitting up of the latter into an amido product which will be oxidised into urea, fat remaining behind if there be insufficient oxygen for its combustion. Another source of fat may be the decomposition of lecithin; concerning this source, however, there is a difference of opinion.

Experimental Pathology of Fatty Degeneration. — Voit and Bauer showed that animals which had been starved, and were eliminating a constant of N in the form of urea, after the administration of small doses of P, suddenly eliminated a great increase of N; while at the same time the oxygen taken in and the CO_2 given out were considerably diminished. These facts are clearly associated with the macroscopic, microscopic, and chemically demonstrable fatty degeneration of the striped muscles, the heart, the liver and kidneys. In 100 parts of the dry substance the ether extract is

	Healthy Dog.	Phosphorismus Dog.
Muscle . .	16·7 per cent	42·4 per cent
Heart . .	9·2 ,,	20·4 ,,
Liver . .	10·4 ,,	30·0 ,,

It might be said that the diminution of O intake and CO_2 output was due to blood destruction, but the experimenters were unable to find evidence of this.

According to Gaule, some of the fat may arise from the formation of lecithin. He maintains that the primary change in phosphorus poisoning is in the nucelus. According to Krehl, only a very inconsiderable portion of the fat in fatty degeneration of the heart arises from this source, and the lecithin is not appreciably increased. Slow poisoning by carbon monoxide produces fatty degeneration. This gas turns out the oxygen, forming a more stable compound with hæmoglobin than does oxygen, and produces the same effect on the tissues as profound anæmia, viz., deprivation of oxygen. But prolonged insufficiency of oxgyen means also a lowered vitality of the cell elements; and it may be that the cause of the fatty metamorphosis of the cell protoplasm in this form of poisoning as well as in phosphorus poisoning can be thus explained. The fact that CO, administered to starving dogs, increases the urea output, shows that there is an increase in destruction of organ proteid and deposition of fat owing to insufficiency of oxygen. The object of using starved animals is, of course, to prove that the increased N must come from tissue metamorphosis. But in phosphorismus the same result is not explained by alteration of the blood; and in my opinion too little stress has been laid upon tissue respiration. We have seen that the cells nourish themselves and, probably by virtue of nucleo-albumins combined with ferric oxide, they have the power of taking up oxygen and storing it in the protoplasm. It is possible that P may interfere with this oxygen storage by the tissues; hence less oxygen could be taken up by the blood, less CO_2 given off, and no appreciable change in the hæmo-

globin value would be evident. Starving animals from whom large quantities of blood have been abstracted pass an increased amount of urea.[1]

Litten showed that rabbits and guinea-pigs, which had been kept three to six days in an atmosphere of 36° C., showed fatty degeneration of the heart, the striped muscles, the liver and kidney. This would seem to indicate that a high temperature maintained continuously in animals which have a relatively low capacity of heat dissipation (thermolysis), produces fatty degeneration, and supports the view that fever may produce fatty degeneration. Experiments upon such animals as rabbits are not always to be accepted as conclusive; and Naunyn has shown that such animals may be kept thirteen days at a temperature of 36° to 40° without any fatty metamorphosis, provided they receive abundance of green food and the warm chamber be properly ventilated. In fever there is certainly increased organ proteid destruction; but according to Krehl, there is no parallelism in man between the height of the fever and the fatty degeneration of the muscles. Much would depend upon the effect of the toxins upon the muscles, the nerves, and their endings in the muscles.

Diseases in which Fatty Degeneration Occurs. — In the different grave forms of *anæmia*, particularly *pernicious anæmia* and *hæmorrhagic purpura*, fatty degeneration of the muscular substance of the heart occurs, whereas other muscles in the body are not affected. It may occur after severe hæmorrhage. We may then ask, Why should the *heart* undergo this degeneration and other muscles escape? Several factors seem to be at work in producing the metamorphosis of the cell protoplasm. In chlorotic anæmia the hæmoglobin value of the blood may fall as low as in pernicious anæmia; yet in the former fatty metamorphosis seldom, if ever, occurs, whereas in fatal cases of the latter it is never absent. Other factors then are present besides deficiency of oxygen. In both diseases the work done by the heart is increased. In pernicious anæmia there must be other causes, possibly one or more of the following: the diminution of the quantity of blood; the alteration in the quality as shown by the great diminution of the specific gravity; the great deficiency of iron in the pigment of the blood, and consequent diminution of the oxygen carrying value; and the presence of toxins in the blood. That many of these factors act together in producing the metamorphosis of the cell protoplasm is clear, and that the heart muscle is selected, and the voluntary muscles spared, proves that not the least important factor is work with inadequate repair of waste; for while, on the one hand, the feeling of languor and indisposition to work, which is a prominent symptom of anæmia, imposes rest upon the voluntary muscles, and therefore a lowered metabolism in conformity with the depressed vital activities of these tissues, the heart on the other hand must, by its automatic activity, do even more work in order to supply the necessary oxygen and

[1] Araki, working in Hoppe Seyler's laboratory, showed that one effect of lessened oxygen supply was the presence of lactic acid in the urine, sometimes of sugar and albumin. Poisoning by CO, curare, and strychnine gave corresponding results, as also after epileptic seizures when the respiration was retarded. Diminution of oxidation processes is a factor common to all these conditions, and doubtless a primary cause of the abnormal metabolism.

nutrition for the nervous system. It would be of interest to see if the diaphragm is similarly affected;[1] for on account of the "air hunger" it must do proportionately more work than other striped muscles. There are, moreover, certain other facts in pernicious anæmia which support the theory of the origin of fat by the disintegration of organ proteid, viz., the abundance of subcutaneous fat and the large amount of N eliminated by the urine — generally more than can be accounted for by the food.

Another frequent cause of fatty degeneration of the heart is *partial occlusion* of the *coronary arteries* by atheroma. A large proportion of the cases of fatty degeneration of the heart in people who have passed middle age are of this origin. Sometimes one or both coronary arteries may be obstructed with or without valvular disease, and the occlusion may be so great that the artery may admit a bristle with difficulty. As one coronary artery, or a branch of one, may be obstructed, the fatty degeneration may be local, affecting only one side of the heart — more often the left which has the most work to do; but the auricles are usually not affected in such cases.

Certain toxic agencies, besides phosphorus and carbon monoxide, produce fatty degeneration, viz., arsenic, antimony, sulphuric acid, nitric acid, chronic alcoholism and, lastly and most importantly, *toxins* — the products of microbic infection and growth.

Finally, fatty degeneration may be the expression of the gradual running down of the vital mechanism: we have supposed that every particle of living protoplasm is endowed with a certain amount of endurance, and when the limit of the life of the cell is approached, fatty degeneration occurs: in this way we can explain the *senile fatty metamorphosis* of cartilage cells and the excess of fuscous pigmentation of the ganglion cells of the central nervous system; most of such pigment being really of a fatty nature. We thus see that fatty degeneration is the result of a lowered vital activity of the cell or fibre, and the conditions which give rise to it are complex, but depend essentially upon — (1) Failure of nutrition of the cell, which makes it unable to compensate the waste by repair; (2) Breaking down of the cell protoplasm and formation of amido antecedents of urea and of fat out of organ proteid; (3) Insufficiency of oxygen-supply by the blood, or incapability of the cell itself to take up sufficient oxygen to oxidise the fat, hence accumulation of a deposit within the cell or fibre.

Fatty Degeneration of the Nervous System. — We have seen how fat can be formed from proteid; can it be formed from lecithin, an important constituent of nervous matter? To this subject I have given particular attention, and I shall therefore set forth at some length the reasons why I cannot agree with Cohnheim in assuming that *lecithin* cannot be so split up as to form a neutral fat. We know that muscle fibres, when separated from their motor nerves, are unable to nourish themselves, and are said to undergo fatty degeneration. If such muscles be hardened in

[1] Just before going to press I have examined the diaphragm in a well-marked case of pernicious anæmia, and found a considerable number of fibres undergoing fatty degeneration.

Muller's fluid, and then placed in Marchi's fluid, the fatty deposit will be stained black. Ordinary adipose tissue treated in the same manner stains black. The fatty matter of the healthy central nervous system does not, but if a nerve fibre be cut off from the cell of which it is an outgrowth, that nerve fibre undergoes Wallerian degeneration, and both axis cylinder, and myelin sheath, when treated by the method mentioned above, stain intensely black. The myelin has undergone a chemical change, and the staining reaction would seem to show that the product was the same as that of degenerated muscle, viz., neutral fat. We know that lecithin can easily be decomposed into glycero-phosphoric acid, stearic acid and cholin; the radicle glyceryl may unite with stearic acid to form fat, the phosphoric acid combine with alkalies, and the cholin be decomposed.

It appeared to me that if phosphorus were diminished in degenerated nervous tissue this decomposition had very likely occurred. I resolved, therefore, to ascertain whether this were the case. To obtain absolutely fair comparison, I had estimated[1] the organic phosphorus contained in two halves of spinal cords in which unilateral degenerations had been produced in one case experimentally, in the other by disease. A man with left hemiplegia from thrombosis of the right middle cerebral artery died three weeks after the onset. The spinal cord was stripped of its membranes, and divided longitudinally down the middle. The right half contained 10·74 per cent of lecithin in the dried ethereal extract: the left half 8·15 per cent. If we allow for the direct pyramidal tract, which was well marked, the loss of lecithin in the degenerated pyramidal tract coming from the right hemisphere would be about 3 per cent.

This chemical change is not complete at once after section of the nerve fibre; it takes from six to twelve days to obtain the black staining, which shows that there is a slow process of disintegration and death. In the neighbourhood large numbers of leucocytes can be seen carrying away the granules of fat. It is possible that extensive degeneration may produce an auto-intoxication; and in many chronic brain diseases — such as alcoholic insanity and general paralysis of the insane — the lecithin of the brain tissue is greatly reduced in amount (Kowalewsky), and the perivascular lymphatic sheaths and subarachnoid are filled with fatty products of its disintegration, staining by the Marchi method like degenerated nervous matter.

Toxins, the chemical products of certain pathogenic micro-organisms, sometimes produce fatty degeneration of the muscles. Dr. Sidney Martin has found intense fatty degeneration of the muscles and segmental degeneration of the nerves to result from injection of the diphtheritic toxin. I have observed intense fatty degeneration of the heart in a case of diphtheritic paralysis, but I could find no degeneration of the nerve trunks. It has seemed to me that toxins which produce degeneration act either upon the motor endplate like curare, or upon the nerve cell; but the effect of the poison is manifested in the former case by fatty

[1] I am indebted to Mr. Percy Richards, F.C.S., for making these examinations; the results will be published jointly, and full details given.

change of the muscle, in the latter by degeneration of the outgrowth of the nerve cell (viz., the nerve fibre), as well as of the muscle. Acute atrophy of the liver is probably due to microbial infection, and acute fatty degeneration of the cells occurs.

Naked Eye and Microscopical Appearances of Fatty Degeneration. *The Arteries.* — Fatty degeneration in this situation is not of importance clinically except when it occurs in the vessels of the central nervous system and retina, as it may in poisoning from phosphorus, etc., and in the grave anæmias, when it may lead to rupture and hæmorrhage.

The cells in the adventitia of the small vessels of the brain are the first to show fat granules collected around their nuclei. Fatty degeneration is seldom met with in the middle-sized arteries, especially those of the limbs; it is very common in the aorta, occurring as opaque, whitish

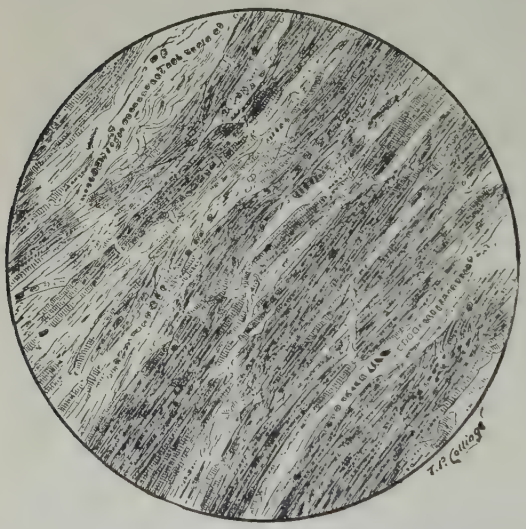


Fig. 9 — Microphotograph of Heart from a fatal case of Diphtheritic Paralysis, stained by the Marchi method, showing *early* fatty degeneration. The fine *black granules* in the fibres are particles of fat stained by the osmic acid. Mag. 250.

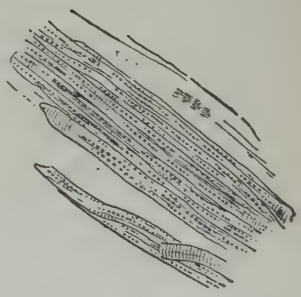


Fig. 10. — A few fibres more highly magnified.

streaks or spots scarcely, if at all, elevated above the surface. The fatty change occurs in the stellate cells of the subendothelial coat; and the tissue thus degenerated may give way so that a very shallow breach of the lining surface is produced.

The Heart. — As before said, the whole muscle substance may be affected, or only the inner surface of the heart, which then assumes a peculiar pale, streaked appearance, seen especially in the musculi papillares and columnæ carneæ of the left ventricle, sometimes in the right ventricle, never in the auricle. This form of degeneration is produced by less severe nutritional defects of the organ; but when there is marked obstruction of the main branches of the coronary artery by atheroma,

idiopathic anæmia, or phosphorus poisoning, the general form of degeneration of the organ exists. The walls of the organ have a yellowish appearance instead of dark red; they are flabby, lacerable, and frequently present a "*tabby-cat*" or "*thrush breast*" appearance. From a large experience in the examination of hearts, I am certain that fatty degeneration may be overlooked unless a microscopical examination be made after staining with osmic acid. I once thus found the organ, in a case of fatal syncope occurring in diphtheritic paralysis, extremely degenerated; yet the heart had been passed as normal on macroscopic examination. It was rather pale and tough but, examined microscopically, the muscle fibres were found to be extremely degenerated: the toughness was possibly due to coagulation necrosis.

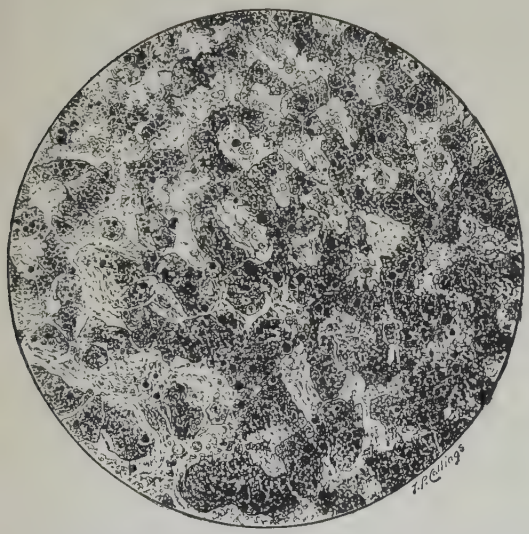


FIG. 11. — Microphotograph of a Section of Liver from a case of Pernicious Anæmia, stained by the Marchi method. The *black granules and droplets of very varying size* seen within the liver cells consist of fat stained by the osmic acid. Mag. 300.

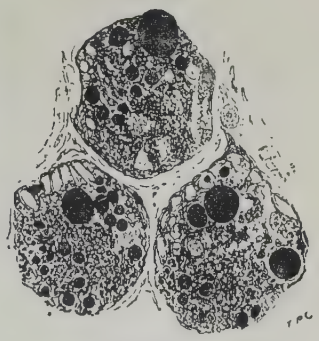


FIG. 12. — A few cells much more highly magnified.

Microscopical Changes in Fatty Degeneration of Muscle Fibres, etc. — The fat granules occur first as fine molecules scattered through the fibre; only in advanced cases do they run together in droplets, and even there they never form drops (*vide* Figs. 9 and 10). At first the muscle fibres do not lose their striation, but as the process advances the striæ become less marked, until eventually they may be entirely lost. Obersteiner has recently described a peculiar form of interfibrillary fatty degeneration of the muscles of the tongue in a case of tabes dorsalis: the hypoglossal nucleus was intact. In the liver cells and renal epithelium the fat droplets vary greatly in size, from fine granules up to drops which nearly fill the cell; so that it is sometimes extremely difficult to deter-

mine whether the liver cells be the seat of fatty infiltration or degeneration (*vide* Figs. 11 and 12).

Fatty changes in the kidney are common, due to secondary degeneration of the epithelium and inflammatory products, *e.g.* large white and small white kidneys [*vide* article "Diseases of Kidney"]. Primary fatty degeneration of the cells of the liver and kidney occurs in phosphorus, arsenic, and antimony poisoning, especially in the first named.

Ziegler has pointed out that fatty degeneration may accompany lardaceous disease.

As the cells of the fixed tissues may undergo fatty metamorphosis, so may the cells of fluids, *e.g.* pus cells; and of coagulated fluids, *e.g.* casts. It was once believed that fatty degeneration was the same process as the formation of adipocere, but Kraus has shown that aseptic tissues can be kept a considerable time without appreciable increase of fat. *Adipocere* is the result of the action of living organisms upon dead tissues, like the ripening of cheese; here compounds of the fatty acid series — caprylic, caproic, and butyric acids — are formed which unite with ammonia and alkalies to form soaps; whereas in fatty degeneration a neutral fat is formed.

Fatty degeneration occurs in atheroma [*vide* article "Diseases of Arteries"]. The *arcus senilis* is usually considered a sign of degeneration. It was formerly thought to be a fatty degeneration occurring in the cornea; but it is shown to be a deposit of matter (fat or colloid material staining black with osmic acid) in the lymph spaces. It very probably comes from elsewhere; as it has been met with in fat young women, it is not a definite sign of degeneration. Fat in cells or tissues can be recognised microscopically by the colourless, highly refractive droplets with a dark contour, insoluble in acetic acid, soluble in alcohol and ether. They stain black with osmic acid. There is no reliable means of distinguishing fatty accumulation within a cell from fatty degeneration. In the latter stages of fatty degeneration, when the cells are dead and in great part destroyed, the whole tissue may be broken down into *an opaque yellowish white detritus* such as occurs in atheroma. In the débris are found characteristic crystals of cholesterine — rhombic in shape, with a corner notched out — and feathery crystals of margarine.

Cloudy Swelling, *parenchymatous or granular degeneration or albumi-*

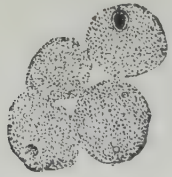


FIG. 13. — Cloudy Swelling of Liver Cells (× 350 diameters). — *Hamilton.*

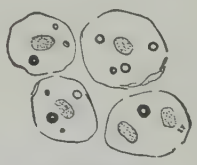


FIG. 14. — Same treated with acetic acid. — *Hamilton.*

nous infiltration, is a condition which often precedes fatty degeneration, and was first described by Virchow as affecting the special cell elements of

organs in a state of parenchymatous inflammation. It is a chemical and structural change in the protoplasm of the cell, or fibre, which becomes swollen and indistinct in outline and structure; the nucleus also is obscured by the precipitation of fine granules of an *albuminous* nature (*vide* Figs. 13 and 14). These granules are feebly reactive to light, hence dusky in appearance; they are not stained by osmic acid, nor are they soluble in ether, but they dissolve in dilute acetic acid and caustic potash: they cannot be fat therefore, although fat granules often coexist as the morbid process advances. It occurs with especial frequency in the specific fevers — typhoid, diphtheria, scarlet fever, etc. — and especially affects the liver, kidneys, heart, and voluntary muscle fibres; but probably all protoplasmic structures suffer. The change is not due to the pyrexia *per se*, but in all probability to the action of the toxins which are producing the fever. Cloudy swelling is the first change noticeable in poisoning by phosphorus, arsenic, antimony, carbon monoxide, and the mineral acids, thus preceding the fatty degeneration. To the naked eye the organs appear swollen and frequently anæmic; the tissue often has a lustreless appearance, but it is softer than natural. The change is well marked in the liver, but its most serious effect is upon the heart: the muscle fibres become slightly opaque, pale, soft, finely granular, and their striæ indistinct; such a condition is frequently found in acute myocarditis.

In acute desquamative nephritis the epithelial elements of the uriniferous tubules, especially of the cortex, undergo cloudy swelling which terminates very often in fatty degeneration.

Calcareous Degeneration. — The blood, the lymph, and most of the tissues of the body contain lime salts; two-thirds of the weight of bone is made up of earthy matter. Calcareous deposition in a tissue may, therefore, be due to precipitation of the lime contained in the tissue, to precipitation of lime normally contained in the blood and lymph, or to excess of lime circulating therein, derived from disintegrative processes occurring in bone (*e.g.* caries, osteomalacia, or senile atrophy). Deposition from this last cause is termed metastatic.

Calcification of a tissue is most frequently a sign of *senescence;* it occurs generally in dead or dying tissue. It is not, however, exclusively an attribute of old age, for it has been known to occur in early life or childhood; a remarkable case has been described of calcification of the middle-sized and smaller arteries in a lad the subject of dorsal caries: calcification does not indeed necessarily depend upon the age of the part, as it may occur in the fœtal tissues of the placenta. It is very prone to occur in dead tissue, and Litten has shown that the process of calcification is intimately associated with coagulation of the albumin of the tissue. "If the renal artery in an animal be ligatured, and the ligature removed after an hour and a half, so as to allow the circulation to return, the only noticeable change is an exudation of albuminous substance into the Malpighian bodies. When the blood has continued to flow for twenty-four hours there is a precipita-

tion of calcareous salts to such an extent that the organ may become as hard as stone."

Calcareous deposits contain calcium phosphate ($Ca_3 2PO_4$) traces of carbonate and minute quantities of magnesium phosphate and carbonate — sometimes very minute quantities of fluoride of calcium and oxide of iron. The mineral matter, therefore, corresponds closely with that of bone. Calcified tissues are readily distinguished from true bone by the fact that when acted upon by HCl and the lime salts thus dissolved out, bone corpuscles and lamellæ are seen to be absent.

Appearances: (1) *Macroscopic Examination.* — Calcified tissue often feels and looks like bone; it breaks with an irregular surface, and presents a yellowish and grayish aspect; this is the case when it occurs in plates or spicules, but owing to simultaneous fatty degeneration of the tissue it may have a mortar-like appearance and consistence: small whitish or yellowish concretions of varying size and form may be seen and felt in the soft detritus (*e.g.* in caseating glands and atheroma).

(2) *Microscopic Examination.*—The infiltration of the lime salts occurs both within the cells and in the intercellular substance, especially in the latter situation, where they first made their appearance as a fine precipitate of opaque, round or irregular granules, which look black by transmitted light. As the process advances these increase in number, until ultimately the structure of the tissue may be lost. Thus portions of tissue may be converted into masses having a black, irregular outline and a homogeneous, glistening appearance. Usually the cell elements of the tissue are enclosed and obscured by the precipitated lime salts; but in some situations (*e.g.* the brain) the ganglion cells are the seat of deposition. The deposition within cells is best studied in this situation. The granules look like highly refractive particles, and are soluble without development of gases in HCl. The nucleus remains free from the deposit, but gradually diminishes in size as the lime accumulates within the cell. The dendrons are often affected, the neuron very seldom. Calcification of the ganglion cells has been found in fractures of the skull, not due, however, to excess of lime in the blood (metastasis) so much as to death of the nerve cells and alterations in the circulation.

Causes of Calcareous Precipitation. — If the lime salts be held in solution by the carbon dioxide present in the blood and lymph, then lowered metabolism of the tissues, and enfeebled circulation, such as occur in senile decay, would by default of carbonic acid favour precipitation of the calcareous salts of the lymph; there is some evidence in favour of this hypothesis: arteries are extremely liable to calcification of their walls, veins are not. Incrustation of the walls of the left heart is common, of the right heart not; calcification of the renal glomeruli which normally contain arterial blood is common. Since the CO_2 tension in the pulmonary veins is extremely low, and yet calcification is never seen in them, there must be other factors which cause precipitation of the lime salts in arteries; such are all conditions which lower or destroy the vital endurance of the tissues forming the walls — occupation involv-

ing mechanical strain, diseases associated with high arterial tension, toxic conditions of the blood (*e.g.* alcohol and syphilis), and lastly old age.

Calcification is very liable to occur in dead, dying or decaying tissues; it is often found associated with or following *fatty degeneration*, especially caseation; *e.g.* atheroma, caseous tubercular glands, caseating foci in the lungs, and old infarctions. Many new growths undergo calcification in the centre, where nutrition is impaired, *e.g.* sarcoma of muscle, fibro-myomata of uterus, carcinomata, psammomata and endotheliomata of the dura mater. Calcification of old inflammatory products, especially when occurring on serous membranes, is not uncommon; and we can thus account for the calcareous plates met with in the pleura, pericardium and peritoneum. The muscular walls of the heart and granulations resulting from valvular endocarditis often are the seat of calcareous deposition; likewise phleboliths of varicose veins are probably calcified granulations or thrombi.

Dead tissues lying in the midst of living tissues are prone to calcification and *petrification*, *e.g.* lithopædium of extra-uterine gestation.

Calcareous infiltration occurs in process of time in abnormal or vitiated secretions of organs. Calcareous concretions are thus met with in the salivary glands, pancreas, tonsil, articulations, and synovial sheaths; and in the interior of cysts (particularly colloid cysts) of the thyroid and kidney.

Results. — As a rule calcification is associated with death of the tissue and loss of function; it is not a cause, but an effect, and always means lowered vitality if not death of the tissue. Calcification of muscle fibres does not necessarily mean necrosis, but it indicates great depression of function.

Calcareous deposition may be salutary, *e.g.* when calcification of the inflammatory products surrounding parasites (such as trichinæ of muscle, pentastoma dent., and echinococcus of the liver) encapsulate the parasite, and either render it inert until the capsule is dissolved in the stomach of another animal, or until it is actually infiltrated with lime and destroyed.

Calcification of the cartilages of old people is not at all uncommon; it is met with in the larynx, trachea and rib cartilages; it is, however, a provisional process prior to ossification. Likewise inflammation or disease of cartilage may be followed by vascularisation and ossification. The comparatively frequent occurrence of bony anchylosis in old people proves clearly enough that if the joints once become fixed from pathological causes, ossification of the articular cartilages will occur.

Pigmentary Degeneration. — The pigments found in the tissues are — (1) Intrinsic — those which normally exist in the body or arise from pigments already in the body. These pigments are either derived from the colouring matter in the blood — *hæmatogenous*, or are *non-hæmatogenous*.

(2) Extrinsic — those which enter the body by the lungs, skin, or alimentary canal.

A pigment containing sulphur, which is probably non-hæmatogenous,

is a normal constituent of the skin in some races and individuals, and consists of blackish or brownish granules contained in the deeper cells of the "rete Malpighii." Under certain circumstances this pigment is increased; for instance, round the nipples in pregnancy and in parts of the skin exposed to the air, and especially to the sun's rays. Intensification of the normal pigment of the skin is met with in certain pathological conditions; notably in Addison's disease, scleroderma, leprosy, tuberculosis, and the cancerous cachexia. In wasting diseases generally the fat has a deep yellow colour, and the muscle assumes a deep brownish-red appearance, due to intensification of the normal pigment. The pigmentation of the skin in Addison's disease, in leprosy, and in scleroderma is probably due to changes in the nervous system (*vide* special articles). Leloir has shown that an atrophy of nerve fibres occurs in parts affected with vitiligo.

According to Unna, the epidermis may take on a brown colour by *keratinization*, a process in which water and oxygen are taken from the cells, and the sulphur relatively increased thereby. He thus accounts for the pigmented appearance presented by the skin in ichthyosis and xeroderma.

Hæmatogenous pigmentation. — A certain number of pigments met with in the body are certainly derived from the blood pigment, viz., the bile pigments, bilirubin and biliverdin, urobilin (which is identical with hydrobilirubin) and hæmatoidin. In pernicious anæmia the peculiar old wax appearance is in part due to urobilin jaundice. All these pigments are iron free, and give a play of colours with fuming nitric acid. When blood corpuscles undergo destruction, as in large extravasations of blood, two substances may be formed — (*a*) *Hæmosiderin* and (*b*) *Hæmatoidin*. The former substance, containing iron, turns black with ammonium sulphide, and gives the prussian blue reaction with ferrocyanide of potassium acidulated with hydrochloric acid; it takes the form of granules of varying size which are frequently found within leucocytes. Hæmosiderin may also be found in the renal epithelium, in the fixed cells of the connective tissue, and also in lymph channels and lymphatic glands, whither it is carried by leucocytes. Organs which are allowed to undergo putrefaction, and contain a large quantity of hæmosiderin, turn black owing to formation of sulphide of iron. This often happens in pernicious anæmia, where a very large amount of this substance is found in the liver owing to disintegration of the red corpuscles. Hæmosiderin in large quantities may be found in the liver and spleen in severe forms of malaria, owing to the destruction of the red corpuscles, and from the action on the blood of certain poisons, such as arseniuretted hydrogen and toluyl-endiamine.

Hæmatoidin, a pigment which is iron free, may be formed from extravasated blood, *e.g.* in apoplexy. The brain substance in the neighbourhood of the hæmorrhage is stained an orange-red colour, and microscopical examination reveals minute orange rhombic plates or granules of hæmatoidin. The deposit of pigment in the skin from

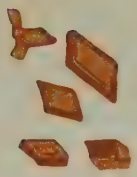


Fig. 1. *Haematoidin Crystals from old haemorrhage into the brain × 400 Diams.*

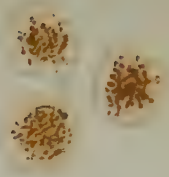


Fig. 2 *Haematoidin granules in liver cells, Cyanotic atrophy of liver × 400 Diams.*

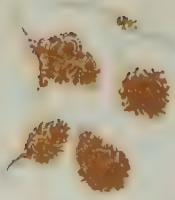


Fig. 3 [illegible]

Fig. 4 [illegible] of coal & soot from [illegible] × 400 Diams

"From Hamilton's Pathology."

changes in the extravasated blood is the cause of the characteristic colour of syphilitic eruptions and ulceration. Recently Treacher Collins has shown that hæmorrhage into the anterior chamber of the eye is followed by a rusty staining of the cornea, due to imbibition by osmosis of blood pigment, and conversion of the same into its derivatives *hæmosiderin* and *hæmatoidin*.

In malaria, in consequence of the destruction of the red corpuscles by the plasmodium malariæ, two kinds of pigments are formed: a pigment contained within the organism itself, black in colour, which does not give the iron reaction; another, hæmosiderin, found in the liver, spleen, and marrow of bone.

Melanin is a pathological pigment which does not arise from the blood; it can only be formed by the action of living protoplasm, and melanotic tumours are found usually to have originated in some tissue the cells of which normally contain pigments, *e.g.* the choroid coat of the eye. Melanin contains no iron, it has a black appearance in mass, but examined microscopically by transmitted light it is of a brownish or sepia colour; it is soluble in alcohol, ether, mineral acids and solution of caustic potash, and is bleached by chlorine; these tests serve to distinguish granules of melanin from particles of carbon, etc. [*vide* Plate].

Various pigments are found normally in the cells of the central nervous system, *e.g.* the locus cæruleus and locus niger; and the ganglion cells of the brain, spinal cord, and sympathetic ganglia of human adults contain a fuscous pigment which occurs in the body of the cell, usually in the neighbourhood of the nucleus. This pigment is seldom present in children, and I have not been able to find it in monkeys and other animals. In young adults it is of a bright yellow colour; in old people it is darker and usually more abundant; it stains black by the Marchi method, and is therefore a fatty derivative. Whether it be really increased in certain diseases, or only more evident on account of atrophy of the rest of the cell substance, we do not yet know; in progressive muscular atrophy many of the cells appear infiltrated throughout with pigments.

Pigments derived from extraneous sources are introduced into the tissues of the body by the respiratory and alimentary systems. *Anthracosis* is the pigmentation of the lungs and bronchial glands caused by the inhalation of fine particles of carbon which are taken into the lymphatics by leucocytes. Most adults have their lungs somewhat pigmented from this cause, but when, owing to occupations such as coal mining, etc., enormous quantities of coal dust are inhaled, the lungs may be absolutely black in colour.

Argyria, a condition of bluish discoloration of the skin, was occasionally seen in times gone by when nitrate of silver was used for long periods in the treatment of epilepsy.

HYPERTROPHY. — An organ is said to be hypertrophied when all

parts of it undergo an abnormal increase, not due to degeneration or to elements foreign to its normal structure.

The term hypertrophy should not be applied to malformations, such as a large finger; or to excessive development of the organism as a whole, the result of congenital influences; but rather to "the enlargement of an organ, partial or complete, beyond its usual limits as the result of increased function or of some unusual condition of the corresponding or correlated organ" (Bland Sutton).

Hypertrophy should, moreover, be distinguished from simple overgrowth, as of uncut hair or nails.

Without increased blood-supply to the part hypertrophy cannot take place, but increased functional activity implies increase of nutrition brought about by vaso-dilation; this in its turn is induced by the stimulus acting on the vaso-motor nerves of the small arteries. In glands there exist definite vaso-dilator nerves; when the gland is active the vessels dilate by the excitation of these nerves.

Functional and Compensatory Hypertrophy. — The increased size of a hypertrophied organ may depend upon two factors; namely, numerical hypertrophy or hyperplasia, and simple hypertrophy or the increase in size of its constituent elements. The two may go hand in hand; for example, the development and increased size of the muscles used in particular occupations or exercises are the result of an increase in size of the fibres due to increased nutrition. "Work-hypertrophy" is a natural attribute of working organs.

Another example of physiological hypertrophy is the gravid uterus, wherein muscular fibres of the organ increase both in number and in size. Kölliker showed that these unstriped muscle fibres are eleven times longer and four times broader than in the normal state. Another example is the mammary gland cell, the elements of which, owing to the physiological stimulus of gestation, undergo hyperplasia.

Compensatory Hypertrophy in Disease. — Of this there are many familiar examples. In dual organs — as the kidneys, testicles, lungs, and ovaries — when, either from congenital absence of one of the pair from disease or from removal, the whole of the particular function is carried on for some considerable time by the other, the latter undergoes compensatory hypertrophy.

Hollow viscera with muscular fibres in their walls afford examples of hypertrophy of muscular substance; *e.g.* the walls of the general cavities of the heart undergo compensatory hypertrophy when increased functional activity is demanded by increased resistance in front: such is the hypertrophy of the left ventricle in chronic Bright's disease, and of the right ventricle in pulmonary obstruction and mitral stenosis. The hypertrophy of the left ventricle in aortic regurgitation may be explained by the increased functional activity and proportionally increased quantity of blood driven into the coronary arteries at each systole. Hypertrophy of the muscular coat of the bladder in stricture of the urethra, of the stomach in stricture of the pylorus, of the

intestines above a permanent stricture, serve as further examples of compensatory hypertrophy of hollow viscera.

Enlargement of the left lobe of the liver, when the right has been destroyed or its growth checked, is an example of *partial hypertrophy* of an organ.

An increase of the lymphatic glands after removal of the spleen affords an example of compensatory *hypertrophy of a correlative structure.* Two factors are concerned in all these functional compensatory hypertrophies: increase of nutrition, owing to increased blood-supply, and the physiological stimulus which excites the constituent cells or fibres of the organ to assimilate more nutriment. A cell is not nourished, but nourishes itself.

The forms of hypertrophy so far described may be looked upon as beneficial — even as physiologically normal; but examples of hypertrophy occur which are essentially abnormal, *e.g.* enlargement of the thyroid in Graves' disease, of the spleen in leucocythemia, of the lymphatic glands in Hodgkin's disease.

I can but allude to a number of curious pathological forms of hypertrophy, namely, leontiasis ossea of Virchow, which is characterised by multiple hyperostosis of the face and cranium; osteitis deformans, in which there is general increase of size with a marked morbid change of structure, in the form of a curious combination of condensation and hardening with softening and rarefaction; hypertrophic pneumic osteo-arthropathy, a curious disease described by Marie. Hypertrophy, or perhaps a pseudo-hypertrophy of the pituitary body, is frequently associated with an enlargement of certain parts, such as the hands, the feet, and lower part of the face, due to an osseous proliferation and new formation of spongy bone (*vide* descriptions of these morbid states in their respective chapters). The causes antecedent to these peculiar morbid hypertrophies are not understood. It is possible that some are due to the irritation of living organisms; for microbes may act upon animal cells, not only in a destructive manner, but as formative stimuli.

Friction or pressure, giving rise to hyperæmia of the cutis vera, causes increased cell proliferation of the epidermis; but certainly this hyperplasia would not occur if the nerves to the part were destroyed. The irritation of the nerve ending serves not only to determine an increased flow of blood to the part, but also increased formative activity on the part of the cells of the rete Malpighii.

Increased blood-supply to a limb may cause lengthening of a bone, of which an epiphysis remains ununited. Further, a chronic venous obstruction leads to excessive transudation from the blood; this does not give rise to hypertrophy of muscular or glandular tissues, but to a fibrous hyperplasia which, as it progresses, may lead to shrinking of the organ at the expense of the essential cell elements. In obstruction to the return of lymph from a lower limb, as in elephantiasis commencing in infancy, the limb not only increases in bulk generally, but, rela-

tively to those of the opposite limb; the bones become manifestly augmented both in thickness and in length.

Hypertrophy of bone has also been produced experimentally in animals by prolonged administration of small doses of phosphorus; and this effect has been attributed to diminished waste: it might also be explained by this substance acting as an irritant, thereby causing increased formative action. "Hyperplasia" is applied only to increased growth of pre-existing elements, normal in type and situation. Regeneration can only occur when matricular cell elements still exist to proliferate, and it must be borne in mind that highly specialised cell-structures — *e.g.* muscle, glands, and the central nervous system — show very little power of regeneration when injured. It is especially the fibrous connective tissues and epithelial tissues which possess capacities of proliferation and regeneration. Large areas of epithelium may be destroyed and yet regeneration occur; and *skin grafting* is a familiar example of the inherent formative activity of the cells of the epidermis.

Cartilage offers an example of a non-vascular connective tissue which is incapable of self-repair; losses of substance are filled up by fibrous tissue. The periosteum, on the other hand, may be looked upon as the best example of the regenerative capacity of fibrous tissue.

F. W. Mott.

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F. W. M.

GENERAL PATHOLOGY OF NEW GROWTHS

SYLLABUS. — *General Remarks on the Pathological Anatomy of Tumours; their Classification; Limitation of the term "Epithelium" Metaplasia; Heterology; Sarcoma; Carcinoma.*

PATHOGENESIS. — *Definition of Tumour impossible; Relation to "Variations"; the three chief Hypotheses, viz.* (1) *Spermatic influence,* (2) *Embryonic residua,* (3) *Irritation; Objections to the first; Illustrations of the second; the Parasite doctrine; Comparison between the clinical course of Malignant Tumour and Tuberculosis; Auto-inoculation; Grafting and Feeding Experiments; Koch's four Postulates; Attempts to cultivate a specific Microphyte; Protozoic theory; Koch's first Postulate, the histological demonstration of a Micro-organism in the Tissue; Koch's second Postulate; Remarks on Treatment.*

General Pathology of New Growths. — (1) *General Considerations on their Structure.* — In no subdivision of Pathology is the contrast between Pathological Histology and Pathogenesis more striking than in the case of tumours.

Of their histology little remains uninvestigated and unknown; of their pathogenesis, though much may be surmised, nothing can be said to be known. For this reason the classification of tumours can at present be constructed only upon an histological foundation. The clinical course of tumours raises a primary division between the benign and the malignant, but nothing is known of the etiological difference underlying the two; it is not inconceivable, indeed, that the difference in clinical history may be referred to a mere histological or anatomical basis.

Histologically all new growths may be classed in two series, viz., those of mesoblastic and those of epithelial origin. In this classification it is most convenient to understand by epithelium tissue of epiblastic or hypoblastic descent; such new growths as arise from endothelium are included in the category either of endothelioma or sarcoma. Although there is not a universal agreement amongst histologists so to limit the use of the word, in the case of tumours such a limitation is of considerable value.

The source of a tumour is the pre-existing tissue — more precisely, the cells of the part in which it arises. Among normal tissues a transforma-

tion of one variety into another has long been recognised, and has received from Virchow the distinctive name of metaplasia. This term is of especial use in the present subject, since it serves to divide such a process from one of degeneration. Such mutations are met with in the whole series of connective tissues, as exemplified between cartilage and common connective tissue, or between connective tissue and bone.

One variety of epithelium, again, may undergo conversion into another; of this many illustrations are furnished during embryonic development, and in after life under various circumstances of irritation or exposure; as, for instance, when in cases of inversion and prolapse within or beyond the vagina, the columnar-celled epithelium of the uterine mucosa becomes transmuted into one of the stratified squamous-celled kind. It is important, however, to notice that elements of epiblastic or hypoblastic descent are never, after their full development or evolution is reached, converted into any of the forms of connective tissue. In the case of new formations a tumour constructed of one variety of connective tissue, say cartilage, may arise from another; under these circumstances the resulting cell growth does not precisely repeat the character of the mother tissue.

Sometimes the "heterology" (Virchow) (1) is apparent only, and is due to the origin of the growth in the embryonic or developmental residues of a tissue with which the new formation is really homologous.

Of this nature may be the striped muscle fibre (muscle plates) in certain sarcomata of the kidney, of cartilage (Meckel's or pinnal) in tumours of the parotid gland, and in chondromata arising within the cancellous tissue of bone.

The most extreme instances of heterology is afforded by the growth of epithelium in connective tissue which is witnessed in the metastasis of carcinoma. Under these circumstances, however, the metastatic formations do not arise from the organ in which they appear, but from the epithelial elements, perhaps chromatiniferous fragments of them, transported to it.

Clinically the great division of tumours, as already noticed, is indicated by the terms innocent and malignant — or simple and infective. The marks characterising malignancy are the infiltration of the surrounding tissues by the growth, and the production of new foci in the neighbourhood of the primary tumour, or in parts far distant; and, as a consequence of this, the local recurrence after operative removal of the primary tumour, or the reappearance of the disease in lymphatic glands or internal organs. Certain of these characters, however, or others clinically allied to them, are encountered occasionally in the case of benign growths. The multiplicity of some benign tumours — *e.g.* soft fibromata, lipomata, cutaneous papillomata, etc. — may equal that of the most malignant. In such cases, however, it is to be observed that the growths in any given instance are confined to a particular system or extension of tissue such as the subcutaneous, the skin, the nerves, the bones, etc.; they do not arise by metastasis from a primary tumour, as they do in sarcoma or carcinoma, but indicate a predisposition confined to

a particular tissue, or mark the incidence of a wide-spread irritation affecting it. Nor is circumscription invariably met with in simple as contrasted with malignant new growths; some soft fibromata are as continuous with the skin and subcutaneous tissue as sarcomata, and certain lipomata are altogether indefinable from the surrounding fat.

The rate and degree of the secondary infection or metastasis is extremely variable, both in sarcoma and carcinoma; and depends (so far as can be at present judged) upon the anatomical relations, vascular and lymphatic, of the primary growth: in the case of "rodent ulcer" metastasis, whether glandular or other, is unknown, howsoever long the local disease persist, and however wide and deeply spread it may be.

Under malignant tumours are comprised the anatomical forms of sarcoma and carcinoma. A **sarcoma** may be defined as a malignant tumour of connective tissue origin, the blood-channels of which ramify between its cells; secondary infection, as a rule, takes place through the blood stream as distinguished from the lymphatic. The histological structure of sarcomata varies within wide limits. In their most typical forms they consist throughout of embryonic connective tissue, round or spindle celled; but this may undergo partial conversion into fibrous tissue, cartilage, or bone — the sarcoma being designated accordingly, fibrifying, chondrifying, or ossifying. This complex character may arise in another manner, namely, by the production of embryonic or sarcomatous tissue out of, that is through the division of the elements of a previously simple tumour.

In either of these circumstances the histological determination of such a new growth becomes extremely difficult; it may be impossible to decide whether it should be named a sarcoma, or regarded as a fibroma in process of rapid growth. The only histological criterion at present available lies in its cellularity; if this be pronounced, and the concomitance of a proper inflammatory process can be excluded, the border line of simple growths is crossed.

By a **carcinoma** is most conveniently understood a malignant tumour of which epithelium forms the essential constituent, *i.e.* tissue of epiblastic or hypoblastic descent. Such new formations are characterised by an alveolar construction, the blood-vessels being confined to the stroma of connective tissue which forms the walls of the alveoli holding the epithelium. It is for this anatomical reason that secondary infection takes place, not by the blood-vessels, but the lymphatics. When the growth arises from an investing epithelium the alveoli are themselves lymph spaces into which the epithelium has bored, and equally so when a carcinomatous glandular epithelium is no longer confined by the basement membrane of acini or ducts.

As a rule the epithelium of a carcinoma retains the type of the normal tissue from which it arises, and the cells even their physiological properties. Carcinomata arising in the ducts of the breast are of the columnar celled variety; in the acini, spheroidal celled; from the in-

vesting epithelium of the nipple, squamous celled: and these characters are repeated in the metastatic growths.

Pathogenesis. — As in other problems of biology, so in the case of tumours, when the basis of any classification is critically examined definition is found impossible; at the best it is merely an artifice by which the mind is aided in the apprehension of facts. So, at the outset it is impossible to define what is to be and what is not to be reckoned as a tumour.

The relation of inflammation to tumour production will be referred to later. But apart from this, tumours pass by insensible gradations into what are by general consent regarded as morphological variations. The line between highly accentuated anatomical tubercles of the bones and osteoma can only be drawn arbitrarily; and certain new formations may be referred to the class of "variations," even though unrepresented in normal morphology.

The life history of many osteomata will justify this. For, unlike most other tumours, their period of formation and growth coincides with that of the rest of the skeleton: they do not exhibit the independence which is so remarkable in the great majority of tumours whether simple or infective; and they may be held as allied in their nature to the abnormal masses of tissue classed as accessory thyroids, supernumerary mammæ, and the like.

Perhaps the best illustration of this is afforded by the fatty accumulations on the buttocks of the Bushwoman. Arising sporadically in a European such would undoubtedly be classed as diffuse lipomata; the buttock, in fact, is a recognised seat of fatty tumours. Yet they are so common among the females of the race mentioned as to rise almost to an anthropological feature. The protuberance itself is regarded as a mark of beauty, which is perpetuated and increased by sexual selection, and probably arose as a variation confined in the first place to a few individuals (2).

Setting aside such a class of new formations, which may be explained as variations not surpassing many of those encountered in the progess of mammalian descent, the theories of pathogenesis may be reduced to the three following: —

1. Spermatic influence.
2. Embryonic residua.
3. Irritation.

1. *Spermatic Influence.* — The first theory views the growth of a tumour as due to the spermatic influence of certain cells upon those contiguous, the latter being, as it were, fecundated and incited to subdivision by the former. Assuming this view to be correct, it would explain only the method of extension, not the origin of a new growth. Whence come the cells which possess the supposed influence? Although difficult tc

disprove in the case of tumours of the connective tissue series, a fatal objection to this view is furnished by carcinomata. The explanation of the secondary formation of squamous-celled or columnar-celled carcinoma in a lymphatic gland by transformation of the leucocytes or cells of the stroma into squamous or columnar epithelium cannot be admitted; there is no histological evidence of it, and it is contrary to the fundamental observations of normal histology. Klebs (3) has suggested that the leucocytes, which are not infrequently met with between and in the cells of malignant tumours, are the spermatic elements. But it is incalculably more probable that such leucocytes are engaged in a process of phagocytosis (they are met with in abundance about the necrosed epithelium of a squamous-celled carcinoma); or that they have been ingested by the larger more vigorously growing cells of the tumour, a fate they meet in the formation of scar tissue where they are consumed by the connective tissue corpuscles.

2. *Embryonic Residua.* — This view, originally foreshadowed by Virchow in regard to chondromata of bone, was extended by Cohnheim so as to cover the whole field of tumour production; on this account it is often spoken of as Cohnheim's theory (4).

It assumes that, during the process of embryonic development, more cells may be generated than are actually necessary for the formation of a particular organ or tissue; and that in such cells, which may remain long dormant, tumours have their source — the embryonic residua retaining their biological potentiality for multiplication.

The theory relates the growth of a tumour to a physiological cause, viz., to the inherent capacity which embryonic tissue in general possesses for growth. That certain tumours so arise can scarcely be denied: the growth of central chondromata of bone is an instance, though here the redundance may affect the growing parts after the date of birth.

We may cite, again, the growth of chondromata from the synovial membranes of joints ("Pedunculated bodies"), where the new formations arise in the groups of cartilage cells contained in the secondary processes of the fringes; for these elements may themselves be regarded as relics of the cartilaginous matrix about the sites of primitive joint-formation, the articular cavities being formed by the solution of the mesoblastic tissue intervening between the primordial cartilage of the future bones. Such chondromata are unknown in connection with the synovial sheaths of tendons or bursæ, or known only in rare cases that allow of explanation. The large adenomata, again, which lie between the rectum and coccyx (sacral or coccygeal tumour), and have their origin in the post-anal gut, may be cited as another example; or the cystic epithelial tumours of the jaws which, as evidenced by their structure, almost as certainly arise in redundant portions of enamel organ: or, among malignant new formations, the melanotic sarcomata which appear in congenital moles, the latter being visible excesses in the development of normal tissue. Beyond the category of solid formations, or tumours properly so called, a large number of cysts have their

source in the remains of canals which should normally disappear or undergo atrophy during development or growth: such are the cysts of the parovarium, of the par-epididymis, of Gartner's duct in the female, or Müller's duct in the male, of the urachus, the post-anal gut, the thyro-lingual duct, and others.

The hypothesis receives confirmation, too, in the woody masses or xylomata which arise in the dormant buds of exogenous trees. Thus it is satisfactory in a certain number of instances, but unconvincing when applied to the whole; for it not only assumes the presence of such residual elements in every case, but it ignores the equally possible action of a continuously working irritant, such as an animal or vegetable parasite would furnish, for which there are equally apt analogies in the various galls of the vegetable kingdom, some of which display a high grade of organisation.

3. *Irritation.* — Under this heading may be comprehended irritative causes in the wider sense, without attempting to draw a line between irritation and inflammation. It is not, indeed, possible to separate tissue overgrowth which arises out of inflammation from the class of tumours; hyperplasia is the immediate result in both. It is in this connection that trauma becomes included in the pathogenesis of new growths. There is, for example, none but an arbitrary distinction between osteoma affecting the facial bones and the diffuse hyperplasia which Virchow has named leontiasis ossea. Some such formations have a traumatic history; others, of recurrent attacks of erysipelas. The local hyperplasias which result from purely mechanical causes pass insensibly into the new formations known as tumours. In this sense tumours may even form around foreign bodies. One of us has described a large example of lamellar fibroma, found between the bladder and rectum, in the centre of which was a small piece of steel, evidently the immediate cause in its etiology: the other factor was probably the accident of a position which the functions of the bladder and rectum make one of incessant movement.

Undoubtedly, however, the most modern development of this irritative theory and the most definite is the parasitic. In the matter of malignant growths more particularly it has much to recommend it, and from this aspect the hypothesis may be discussed more fully than either of the preceding. It has been urged that, if true of malignant formations, benign growths must be relegated to a like cause. This by no means follows. Cohnheim's theory is equally adequate to account for certain new formations; and there is no *a priori* reason why all should arise from an identical cause. The great feature of malignant tumours is their metastasis, or, to adopt the parallel furnished by the infective granulomata, their infectiveness. The clinical history of a case of sarcoma or carcinoma is so closely like that, for example, of tuberculosis, that it is quite within the truth to assert that there is no feature in the last-named disease which is not paralleled in the others, as will appear from the following considerations: —

The primary tumour in the case of carcinoma is seated most fre-

quently, as statistics show, at sites where an infection from without would most readily take place. The metastasis by lymphatics or blood-vessels in carcinoma and sarcoma is such as occurs in tuberculosis; and it may be restricted to the lymph-glands, or be as wide-spread as a generalised tuberculosis (general sarcomatosis or carcinomatosis).

Even the glandular infection which occurs at times in tuberculosis without primary lesion has its counterpart in the squamous-celled carcinoma of the inguinal glands in chimney sweeps, in whom there may be no discoverable primary growth on the penis, scrotum, or lower limbs. And the latency of glandular infection is equally represented in tuberculosis and carcinoma: a breast, for example, is removed for mammary carcinoma, and four years later, without any local recurrence, the axillary glands may be found diseased. A tubercular lesion may result from direct infection, or may appear primarily in an internal part, *i.e.* in a situation other than cutaneous or mucous surface. The sarcoma that grows at the end of a long bone after injury is comparable with the tubercular osteitis ensuing under similar circumstances. Injury is the determining cause; the other factor is a "constitutional" one. Whether the latter named be held to consist in a congenital want of resistance to an infective virus, or in the actual presence, acquired or inherited, of the virus in a resting or latent condition, the hypothesis equally suits both forms of disease. In short, the abstruse problems of predisposition and heredity offer the same difficulties in malignant neoplasms and in tuberculosis.

Auto-inoculation from one carcinomatous labium to the other has long been recognised; and an instance is authenticated of the transference of carcinoma from an ulcerating tumour of the breast to the skin of the paralysed arm in contact with it. The many examples of intestinal (*e.g.* cæcal) carcinoma associated with numerous lesser growths in the colon; of gastric carcinoma associated with similar disease of the bowel; of œsophageal carcinoma associated with that of the stomach, or of multiple growths in the œsophagus itself, point also to the possibility of an auto-inoculation of the same kind as that of the intestine witnessed in tubercular phthisis. Strictly speaking, however, such facts only show that the disease is transferable in the same individual without proving that a parasitic virus is present in the cells transferred. Although both carcinoma and sarcoma have been grafted from one animal to another, success has as yet only attended the experiments made between animals of the same species. No authentic instance (*i.e.* none satisfying modern criticism) is at present forthcoming of the grafting of human carcinoma upon any of the lower animals. One of the best examples of transference from animal to animal is recorded by Hanau of Zurich, who has successfully engrafted squamous-celled carcinoma from a rat, with such a growth on the vulva, upon a series of other rats, by inserting portions of the tumour into the peritoneal cavity. In one case, where death ensued after three months, the abdominal cavity was filled with nodules which presented the typical histological structure of squamous-celled carcinoma.

We have ourselves carried out a considerable number of such experiments between the human subject and lower animals (5). Our method consisted in transplanting portions of tumours recently removed by operation into the abdominal cavity, subcutaneous tissue or muscles. The tumours used were twenty-three scirrhous carcinomata of the breast and six sarcomata: the animals were monkeys, dogs, rabbits, white rats, three sheep and one cat. At times the entire tumour was placed in the peritoneal cavity after the superfluous fat had been removed from its exterior. On other occasions portions were cut from it and pushed in different directions into the abdomen. The tumour after its removal was kept at the body temperature in an incubator, and transferred to the animal in from half an hour to an hour and a half after removal. Sometimes pieces of as many as three different tumours were placed at different dates into the same animal.

The result of all these experiments was negative. The pieces of transplanted tumour invariably underwent coagulation necrosis, in one case subsequent calcification, and were found either lying encapsuled in the tissues, or to have been completely absorbed. In two instances an entire scirrhous carcinoma of the breast inserted into the peritoneal cavity (dog) entirely disappeared, the abdominal wound having itself healed without discharge of the graft. In the first of these the tumour was one and a half by three-quarters of an inch; the animal was quite well 700 days after the experiment, and, on its being killed, all the viscera were found healthy.

The same negative results attended certain feeding experiments carried out on white rats. We fed two white rats, male and female, with fourteen fresh scirrhous carcinomata. The experiments extended over a period of seven months, during which the animals remained well and several litters of young were born. They were undertaken to ascertain whether infection of the stomach or intestines, such as ensues in some instances from the ingestion of tuberculous material, could be induced. On killing the rats the pylorus and other parts of the alimentary tract were found to be quite normal. In one experiment a small piece of the growing edge of a recently removed scirrhus of the breast was inserted into the anterior chamber of a rabbit's eye. The corneal incision healed perfectly, but the graft, after undergoing slight diminution in bulk, remained unchanged; two months later, on killing the animal, it was found adherent to the iris by one aspect and to the back of the cornea by the other. In all this the experiments, both negative and positive, indicate not the common order of infection, but that of grafting, whether in animal or vegetable tissues. They do not prove, when successful, that the cause of cancer is a parasitic virus, but only that a portion of a malignant tumour will continue to grow in the body of a second individual as it would have done in the body of the first. Even when the spot has been previously prepared by an experimentally caused inflammation, no other result has yet been obtained; as in Mr. D'Arcy Power's experiments of placing pieces of

human scirrhus into the vaginæ of rabbits previously kept irritated or inflamed by the application of linimentum iodi.

Finally, if the positive results attained do not prove the existence of a parasite, it must be borne in mind likewise that the negative do not disprove it. The method of transmission in infective diseases is not always so direct and simple as such grafting experiments presuppose. It has been shown, for example, that malaria cannot be transmitted between birds by the injection of blood containing the hæmatozoon; and we ourselves had found that psorospermosis could not be induced in the scarified skin of the rabbit by rubbing in psorospermial material obtained direct from the livers of other rabbits.

The endemic location of cancer, comprehending sarcoma and carcinoma, is a highly remarkable fact in the history of malignant tumours. One of the most noteworthy instances of it is recorded by Mr. Law Webb. In a group of cottages forming a certain village in Shropshire nine cases of cancer had been treated in fifteen years. The dwellings are grouped together, and do not occupy much more than an acre of ground. All the inhabitants use water from a certain pump situate by the roadside, and close to a very filthy hovel. There are twenty houses in all; one cottage, enjoying a bad pre-eminence for dirt and discomfort, furnished three of the nine cases. In none of the whole series were the patients related by blood.

In the neighbourhood of this hamlet are two houses under one roof with a drain system and water-supply common to both. Calling these Nos. 1 and 2, twenty-six years ago a man, æt. 28, living at No. 1, suffered from cancer of the rectum, of which he died. The house was next occupied by a man and wife. The former, two years after the death of the previous tenant, was treated for cancer of the stomach, to which malady he succumbed. His widow continued to live in the same house, and died ten years later from cancer of the rectum. Before her death a woman in house No. 2 was found to be suffering from carcinoma of the breast, which proved fatal in eight months. The first house was next occupied by three spinsters, one of whom died of cancer of the uterus, and a second with cancer of the stomach.

In connection with the high mortality which obtains in Devonshire we may cite a remarkable instance, the details of which were communicated to us by Dr. R. Ackerley of Surbiton. In a large house in Ashburton, situated on low ground, the cellars of which are below the level of a small stream which runs through the town about twenty yards from the house, four cases of cancer have occurred in the last thirteen years: (1) A lady who had occupied the house for many years died from cancer of the breast; (2) The next occupant, after residing at least seven years in the same house, died from the same disease; (3) her husband died two years ago of carcinoma of the larynx; (4) the second wife of the last mentioned, whom he married five years ago, has lately had her breast removed for scirrhus. Four other deaths from cancer have been certified

in the last four years in persons who had long resided within a hundred yards of the same house.

Cancer has, moreover, a certain geographical distribution. Its distribution in England and Wales has been carefully drawn out by Mr. Haviland (7). His conclusions are that the disease is most prevalent along those river courses which seasonally flood their banks, such as the Thames, the Severn, the Mid Devon and Yorkshire rivers; and that wherever, from the nature of the rocks forming the water-shed, the floods are much discoloured by alluvium, and where, from the flatness of the country, the floods are retained and not easily drained off, there is found the greatest mortality from cancer. [*Vide* art. on Med. Geography of Gr. B.]

Koch's Four Postulates. — Notwithstanding the negative results of the inoculations detailed, the parasitic theory of malignant new growths is so well grounded that during the past few years the whole of the work on the subject has been directed by it.

After the rise of modern bacteriology the first attempts made were to cultivate a specific microphyte from such tumours. In this country we undertook a considerable series of such experiments (8). We confined ourselves to the use of spheroidal-celled carcinoma of the mamma, for the reason that in external carcinomata the problem is complicated by the chances of a saprophytic or adventitious infection; in three instances, however, sarcomata were employed. The media comprised nutrient gelatine, nutrient agar, human blood serum obtained from placentæ, etc., and fluid media, such as hydrocele fluid and human placental blood serum. Portions of the tumour immediately after its removal were cut by means of knives previously sterilised by heat, and transferred to the tubes of nutrient media on the loop of platinum wire. In some cases the tubes were incubated at the body temperature; in others kept at that of the room. The results were uniformly negative, with a few exceptions due to accidental contamination from the air or otherwise during the manipulations the experiments involved.

Although different conclusions have been reached by certain continental observers, it is now universally admitted that these were based on experimental error. Up to the present time no specific microphyte has been cultivated from malignant tumours.

The failure of evidence in this direction led to the suggestion that the hypothetical microparasite might belong to the animal series, and be a protozoon.

In considering this new phase of the problem, the fulfilment of Koch's four postulates must equally be insisted upon. In the case of malaria, it is true, no culture of the hæmatozoon has at present been accomplished, and yet the causative rôle of the latter is accepted; but here the existence of a living protozoon in the blood does not allow of denial. In the case of cancer, on the other hand, this, *Koch's first postulate*, namely, the demonstration of a microzoon in the blood, juices, or tissues, is itself in dispute. In sections of carcinoma there are certain appearances which are interpreted by different observers as indicating the presence of

a protozoon. A full historical account of the minute histology of carcinoma in this relation is given by Noeggerath up to the close of 1891. The more important observations since then are those of Soudakewitch, Foa, and, in this country, of Ruffer. The work of Ludwig Pfeiffer is an attempt to compile the life history of a protozoon from the study of sections of malignant tumours, but the histological misinterpretations it contains are so numerous as to destroy whatever value it might otherwise have. Ruffer has simplified the subject by reducing the hypothetical parasite to a very few definite forms, and we may here cite his description, to the accuracy of which we can ourselves testify. As seen in the protoplasm of the epithelial cells of the growing edge, say of a mammary scirrhus, the fully-grown parasite consists essentially: —

(1) Of a central round, oval, or slightly irregular nucelus, sometimes connected by fine delicate rays with the periphery.

(2) Of a variable amount of surrounding protoplasm, almost, if not quite, filling a capsule (now and then the protoplasm exhibits a series of peripheral granules).

(3) Of a doubly contoured capsule confining the whole.

What of its life history, and especially its mode of reproduction?

If we turn to the more thoroughly known of the microzoa parasitic in the lower animals, a distinct life history, often a very complex one, is to be traced; and a portion of this may be passed outside the body of the host.

The multiplication of the bodies described in carcinoma is alleged to take place by binary division, and groups of considerable numbers may be met with in the epithelial cells.

Certain appearances characteristic of a protozoic life history have been described, such as falciform spores and spore cysts.

As to the former, the opinion of Metschnikoff has yet to be controverted, viz., that the appearances in question result from nuclear degeneration. Indeed, bodies of similar forms may be seen in degenerating tissues from sources altogether different. Other such particles within the cell body pertain to the nuclei of ingested leucocytes or lymphocytes, and yet smaller ones possibly represent the residua of chromatin resulting from the irregular mitoses so frequently observed in the epithelial cells of carcinoma.

As spore cysts have been described —

(1) Aggregations of polynuclear leucocytes in spaces between the epithelial cells, such as may be produced in the rabbit's vagina after repeated application of linimentum iodi.

(2) Cell invaginations, the protoplasm of which is highly vacuolated and the cell membrane unusually pronounced; and, as free spores, the particles resulting from degenerative fragmentation of the nucleus and destruction of the cell.

In squamous celled carcinomata the keratinising cells themselves have been erroneously viewed as parasites. The disproof of this is furnished by the readiness with which every intermediate phase may

be traced between normal epithelial cells and those which cease to take any nuclear stains.

As to the particular body in question, it closely approaches certain of the results of hyaline degeneration the products of which are equally distinguished by their affinity for fuchsin, and are met with, as was shown by ourselves, in various non-cancerous formations, diphtheritic tonsil, caseous lymphatic glands, etc. (14). One test the body in question certainly stands — that of constancy; it may be demonstrated in the growing edge of every carcinoma: and nothing identical has, in our opinion, been hitherto produced in epithelium by artificial methods of irritation.

The bodies seen in the epidermis raised by a common blister stain with differential dyes like nuclear chromatin (those of carcinoma stain in general like the nucleolus); they lie in spherical spaces in the cell body; and, what is most important of all, there is no other structure in the cell representing the nucleus; they are, in short, shrunken nuclei lying in peri-nuclear vacuoles, possibly compressed by the accumulation of fluid around.

As related to the first postulate of Koch, reference may next be made to certain questions in the chemistry of carcinoma. It has been shown that the capsule of encapsulated protozoa consists at times of chitin or of cellulose — both of them substances altogether absent from the tissues of vertebrates. Is either present in a carcinoma? This question can be answered in the negative. The investigation was carried out for us by Gregor Brodie at King's College, London, under the direction of Professor Halliburton, as follows: —

Method. — The tumour is cleared of surrounding fat, but the growing edge is carefully left; it is then minced on a sheet of glass, and boiled in 20 per cent solution of caustic soda for ten minutes, the tissue being in this way dissolved; whilst hot the fluid is filtered through asbestos, the process being hastened by means of a vacuum pump. A yellowish residue, indicating the presence of fats in excess, remains on the surface of the asbestos. Should chitin or cellulose be present it would also remain on and in the asbestos, seeing that it is insoluble in caustic soda. Boiling caustic potass (5 per cent) is run through the filter, and then 20 per cent of the same boiling solution; the precipitate on the asbestos is next washed with boiling distilled water. Nearly the whole of the precipitate, or at least of the pale yellow portion, disappears in this process. The caustic potass is then neutralised by drawing through the asbestos 10 per cent hydric sulphate, first cold and afterwards boiling, and finally boiling distilled water in order to remove all trace of the acid. The presence of chitin or cellulose is now tested thus: —

Cellulose is soluble in concentrated hydric sulphate, chitin in concentrated hydric chloride. A small amount of hydric sulphate is poured on the filter, and after five minutes drawn through. The addition of distilled water to the pale brown filtrate gives a precipitate. The fluid is then filtered through the asbestos, the precipitate appearing on the surface of the latter as a pale yellow film. Were cellulose in solution in

the clear filtrate, it would be demonstrable by boiling the fluid in order to convert that substance into dextrose or grape sugar, which is recognisable by boiling with Fehling's solution. No reaction, however, with Fehling's solution is obtainable.

To remove any fatty acids remaining, or constituting the precipitate on the asbestos, the latter is washed with cold alcohol, hot alcohol, and finally warm ether; a film of faint brown colour still remains on the filter. The test for chitin is next carried out. Chitin is insoluble in strong hydric sulphate, but soluble in strong hydric chloride.

Concentrated hydric chloride is poured in small quantities on the filter, and the filtrate tested; dilution of part with water gives no precipitate of chitin; the remainder is evaporated in a capsule over a water bath; the thinnest pale yellow film remains on the side and bottom of the vessel. This alcohol at once dissolves, proving it to be fatty acid remaining over from experimental error.

Is there albumose in a carcinoma?

We were induced to look for such a body in consequence of its discovery in cultures of pathogenic bacteria; it seemed to us that a like substance derived from the agency of a specific micro-organism might possibly exist in malignant growths.

The method adopted was as follows: —

The tumour, scirrhus of the breast, is minced and pounded in a mortar with 50 per cent glycerine and distilled water, to which is added a little thymol. Before applying the test to the extract, it is ascertained that the reaction is not acid, and that no trace of decomposition is present. An equal bulk of trichloracetic acid (10 per cent solution) is added, and the mixture boiled five minutes in a beaker to bring about the precipitation of the globulins and albumin; it is then filtered. The direct albumose tests next applied to the clear, faintly opalescent filtrate are negative in result.

A drop of strong hydric nitrate gives no precipitate; cupric sulphate solution gives no precipitate; caustic potash solution gives, after the addition of the latter, not a rose colour (albumose), but a violet — an ordinary proteid reaction possibly due to a trace of acid albumin not precipitated by the trichloracetic acid (Brodie). Two possible fallacies may be here noticed. If putrefaction be allowed to arise before the application of the test the ordinary albumose resulting from that process would have been formed. There is, however, a more subtle source of possible error. The reaction of a carcinoma or sarcoma immediately after removal is alkaline; in a few hours it becomes acid: in this the morbid tissue resembles those of the body in general — not only muscular, but glandular also. In muscle a post-mortem formation of albumose is actually brought about by the acid reaction allowing the pepsin, which circulates in small quantity through the body, to digest the proteid. It is quite possible that a trace of albumose might thus be formed after tissue-death if the examination of the growth be deferred.

Koch's Second Postulate. — Seeing that no spores or other indispu-

table evidences of a protozoon have been histologically demonstrated in malignant tumours, the proof of a parasite must depend upon its cultivation outside the body. And it is in this direction that our own latest work has lain (15). We were induced to carry it out, also, for the theoretical reason that the want of success attending the transplantation of carcinoma from man to the lower animals might be due to the fact that it was necessary for the parasite to assume a phase outside its host in order to transmit the disease. Although at one time we employed fluid media in test-tubes, very dilute broth, very dilute agar, milk (to all of which 6 per cent glycerine was added), potassium oxalate plasma (dog), we ultimately abandoned these methods as not ensuring sufficiently natural aëration.

We also fed worms with pieces of mammary scirrhus placed in sterilised sand and water, with the idea that it might be necessary for the hypothetical protozoon to pass through the body of some lower form in order to acquire an infective quality for man and animals. The experiment failed; although the cancer was devoured the worms died, doubtless because the sterility of the sand had deprived them of all other kinds of nourishment.

Again, we buried mammary carcinoma in garden soil and subsequently inserted portions of the tumour (exhumed after six weeks) into the abdomen of rats, but without obtaining any positive result.

Our final method of experiment consisted in the use of sterilised sand and water as a culture medium, and of deep capsules of different diameters as well as Petri dishes, in the place of test-tubes. Portions of the growing edge of the tumour were cut with knives previously sterilised by heat, and then transferred to the sand in the neighbourhood of a littoral which was made by so tilting the sand that the water did not completely submerge it. The capsules were afterwards stored in a laboratory between sterilised double dishes, the covers of these being raised for a short distance with wooden blocks soaked in solution of corrosive sublimate. From most of the smaller deep capsules the covers were removed as they were placed between the double dishes; the Petri capsules were kept covered throughout. Occasionally a small quantity of beef peptone broth was added to the water. The examinations were conducted by removing some of the sand from the littoral in the neighbourhood of the pieces of tumour with a sterilised glass rod to a sterilised slide; the sand so removed is gently stroked with the rod, the slide being so inclined that sufficient fluid leaves the sand to make a microscopic preparation. Many such experiments were made both with mammary carcinoma and different sarcomata; most of the latter were of the melanotic variety from recently killed horses.

In all the experiments carried out with carcinoma we confined ourselves to the typical scirrhus of the breast for the reason that, in the case of new growths involving superficial parts like the lip or tongue, there exists the possibility of infection with purely saprophytic protozoa; some

of which occur normally in such mucous canals as the vagina and intestine.

The examinations were made at different intervals up to periods of five months. In none of the series were any indications of protozoic life encountered. Active amœbæ were found on four or five occasions in different Petri capsules infected with mammary scirrhus and squamous-celled carcinoma; but this observation was limited to the earlier experiments in which the sources of fallacy were not rigidly excluded. In all cases a growth of bacteria ensued, and the purpose of adding broth to the fluid was to favour this, in order that pabulum might thus be furnished for the growth of any protozoa present.

It need hardly be said after this that infection experiments carried out upon animals by means of such sand, or the grafting of portions of tumours incubated in fluid media, have yielded negative results in our hands, whether the sand were introduced into the venous current in dogs, into the peritoneal cavity of rats, or rubbed weekly for many months into the scarified skin.

In the various experiments so performed the sand actually used was teeming with amœbæ, which later observation proved to be adventitious and non-pathogenetic. Similar experiments made with sand infected with the pump-water from the cancerous village referred to in the earlier part of this article were likewise negative; nor did the feeding of white rats with food to which this water was added lead to any different result.

Treatment. — It would be outside the purpose of the present article to deal with the operative procedures practised in the surgical treatment of cancer, or to do more than mention the chief remedies which have been tried from time to time in the treatment of malignant disease. In considering this subject the occasional spontaneous disappearance of certain tumours must be borne in mind. Such a disappearance has been observed not only in benign growths, like fibro-adenomata of the breast and uterine myomata, but also in sarcomata.

In the museum of St. Bartholomew's Hospital, London, is the cast of the head of a man twenty-four years of age, who about six years before admission was struck with the fly-wheel of an engine; a few months later a tumour commenced to grow at the stricken spot, and after reaching the size of a sparrow's egg disappeared in about the space of six months. Six or eight tumours which subsequently grew in different situations on the head afterwards diminished in size. On his admission there was a large tumour near the middle of the anterior border of the left parietal bone, its longest diameter being five inches; and in addition the six or eight smaller growths before mentioned. The chief formation was excised in March 1890, and histologically presented the structure of a fibro-sarcoma. Mr. Butlin has recorded the partial disappearance of what was presumed to be a sarcoma of the testicle in a boy. In this case tumours previously removed from the forehead and front of the ear exhibited the structure of round-celled sarcoma; both testicles subsequently enlarged, but the right afterwards

underwent marked diminution in size; many growths appeared about the same time in various other parts of the body: the administration of mercury had not the slightest effect. It is not impossible that the above case was one of malignant lymphoma or generalised lymphomatosis, rather than of true round-celled sarcoma; the partial disappearance of such formations is a well-known clinical phenomenon, especially during the administration of arsenic.

Considerably more voluminous growths of a tissue that has been by some compared with sarcoma, though it has histologically the structure of granulation-tissue (granuloma fungoides), have been known to undergo complete disappearance quite independently of any local treatment. The difficulty occasionally presented in the differential diagnosis of malignant tumours and syphilomata must also be borne in mind.

As a matter, possibly, of interest we may state that, in search of a protective vaccine, we have tried the effects of subcutaneous injection of a 50 per cent glycerine extract of both carcinoma and sarcoma, hopeless cases being selected for treatment.

The injections in one case of mammary carcinoma exceeded fifty in number, no less than ten different carcinomata being employed. In one instance of recurrent sarcoma of the mamma the glycerine extract of four different sarcomata was used. No local reaction ensued, such as is observed after the injection of "tuberculin" in cases of tuberculosis; and the procedure in no case retarded the growth and multiplication of the tumours. The use of fresh sheep serum was equally inefficacious in carcinoma, *i.e.* the serum of an animal in which malignant disease is so rare that it may be considered to enjoy a natural immunity. Amongst other methods may be recounted Fehleisen's inoculation of erysipelas, the interstitial injection of methyl violet, the passage of electric currents, and more recently the injection of the combined toxins of streptococcus erysipelatis and bacillus prodigiosus (Coley). The effect of the last-mentioned treatment, like that of Fehleisen, is a local and not a general one.

The serum of animals into the circulation of which cancer juice has been introduced has also been used therapeutically. This method we based upon the results obtained with serum antitoxins in general, and we are at present engaged in putting it to the test: the same idea has independently served as a basis of recent work abroad.

Up to the present the only hope has lain in early removal before the infective elements of the tumour have been widely transported into the surrounding tissues or to distant parts of the body. The most successful operator is he who, knowing the pathology of the disease, appreciates the value of free and careful excision. The incisions must be planned to pass through parts believed to be healthy, no knife which has been infected with the juice of the tumour must be used for the division of healthy tissues, lest the seeds of recurrence be sown along the fresh cut surfaces, and not only must lymph glands be removed, but lymphatic vessels. In certain localities the operation for cancer conducted on these principles may permanently rid the patient of the disease. Excision of carcinoma of

the lip may be completely successful; so, in a certain percentage, is that of mammary carcinoma, whilst the free removal of the rectum is followed by better results as regards respite from recurrence than that of any other part.

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PRINCIPLES OF DRUG THERAPEUTICS

I. Introductory

The work of the great Italian anatomists, Vesalius, Fallopius, Eustachius and others in the latter half of the sixteenth century, led eventually to the overthrow of the Galenic system of drug therapeutics; but the influence of the anatomists in this direction was by no means immediate. The early editions of the London *Pharmacopœia*, which was first published in 1618, probably indicate fairly well the method on which drugs were used in England at that day for the cure of disease. In that of 1632 most of the formulæ are copied from the works of Greek and Arabian physicians,—from Galen, Avicenna, Rhazes, Haly-abbas and Mesue,—the name of the physician being given in each case at the head of the formula. Some, however, are of more modern date; John of Arderne (1370) is responsible for two compounds, and from Fernlius many are derived. We note many substances and processes introduced by the alchemists; vitrum antimonii and acetate of lead, for example, are amongst the remedies, and several of the preparations are made by dis-

tillation. We also see the influence of the discovery of the New World on medicine, for guaiacum, cubebs, sarsaparilla and sassafras are amongst the official substances. There is a great variety of compounds; almost all are very complex, many of them containing 30 to 50 ingredients; into the "Antidotus Magna Matthioli Adversus Venena et Pestem" there enter 131 ingredients. There was certainly no lack of curative agents; in the list of simples we find 160 roots, 30 barks, 16 woods, 220 herbs, 90 flowers, 96 fruits, 136 seeds, and 50 gums; besides juices and some other special parts of plants. The animal kingdom furnished 190 items. The fat of 22 animals, the excrement of 11, and the urine of 5, occupy places in the official list of remedies; man is included in each case. Sweat was an official remedy, so too were the ossa triquetra of the human cranium. The brains of the leopard and of the sparrow, the lungs of the fox, and the body of the viper are found among the official animal substances. Sixty syrups and 180 waters were official.

The discovery of the circulation by Harvey, and the advances made in the knowledge of the structure and functions of the body by Willis, Glisson, Malpighi, and others, together with the advancement of chemistry and physics, led, during the seventeenth century, to the formation of new hypotheses concerning disease and its treatment. Van Helmont taught that life was connected with the presence in man of a kind of personal spirit (Archeus), which from its seat in the epigastrium presided over the functions of the body. This Archeus sometimes went wrong, owing to external or internal influences, hence diseases arose. Later we find chemical and mechanical theories of disease. By Sylvius and Willis acidity and alkalinity, or fermentation in the fluids of the body, were supposed to cause disease; whilst Baglivi and other Italian observers, and still later Archibald Pitcairn in this country, laid chief stress on the mechanical changes connected with the tissues and the circulation as causes of disease. All the advocates of these theories either contributed something to the knowledge of the treatment of disease by drugs, or by their works instigated further inquiry: to Willis and Sydenham we owe the greatest advances.

Willis was one of the first to lay stress on the importance of a knowledge of the structure of the different organs as a guide to the use of drugs; and in his *Pharmaceutike rationalis* (1676) he first gives an account of the minute structure of the alimentary canal and its various parts, and of the arteries; he then describes the action of emetics, cathartics, diuretics, diaphoretics, cordials, hypnotics, and opiates. Further on he deals with the lungs and bronchial tubes, and the changes in respiration in diseases such as phthisis, hæmoptysis, and other lung ailments, giving the indications for treatment and the remedies which in his opinion answered these indications. He likewise points out what he regards as the rational treatment for jaundice, ascites, tympanites, and anasarca. In a third portion of the work he deals with the causes and treatment of hæmorrhage, and with blisters, issues, etc. The practical outcome of the work of Willis

was of less value than the spirit of his teaching; his pathological ideas about animal spirits and fermentation as causes of disease were very crude; he was much influenced in his conclusions by old theories of the action of morbid materials, and the indications of the qualities (heat, cold, etc.), of drugs; above all, he too readily supposed that the drugs under which his patients recovered had cured them. His prescriptions are complex, and contain not only a large number of useless agents, but such remedies as the human skull, viper's flesh, millipedes, etc. Yet when he dealt with subjects controlled by anatomical knowledge, he made valuable additions to the existing therapeutical means.

Sydenham professes to recognise the value of anatomical knowledge, but we find little of it in his work. Like Hippocrates, he sought to aid the natural progress of those changes or "commotions" in the blood and fluids of the body which he regarded as the causes of acute disease, and to help nature in her struggle to remove morbid matters. He advocated the removal of the immediate causes of disease, but had no belief in the possibility of dealing with remote causes. By close observation he attempted to determine definite lines for the administration of drugs; he also sought to discover specific remedies, such as he held cinchona to be for ague. He preferred vegetable drugs to animal or mineral, because the animal are too like, and the mineral too unlike the tissues of the body. His prescriptions were more simple than those of Willis, and they are almost free from absurd constituents. But if we examine the prescriptions of both Willis and Sydenham we cannot but see that, with the exception of emetics, purgatives, bitters, and carminatives, very few of the drugs they used had the powers which were claimed for them; and that the art of medicine suffered no loss when a large proportion of the drugs in which they had faith were consigned to oblivion. Under such circumstances we cannot be surprised that the Pharmacopœia of the middle of the seventeenth century showed no signs of improvement. In that of 1677 we find the drugs and compounds almost as numerous as in the Pharmacopœia of 1618; indeed some of the remedies in the latter are even more extraordinary than any in the earlier Pharmacopœia. Not only is human urine set forth as a remedy, but care is taken to distinguish Urina hominis pueri impuberis from Urina hominis adulti!

It is interesting to note that in this Pharmacopœia we find for the first time jalap, serpentary, digitalis and cinchona; and that the names of Galen and the Arabian physicians cease to appear at the head of the formulæ copied from their works.

At the end of the seventeenth century the theories of Boerhaave, Hoffmann, and Stahl considerably influenced therapeutic practice. The two former looked on health and disease as the outcome of chemical and physical conditions acting on tissues endowed with vital properties, which Hoffmann thought due to the presence of an ether-like fluid existing both in the solids and the blood; Stahl attributed everything to soul or spirit. Though both Boerhaave and Hoffmann looked upon

the solids of the body as playing an important part in disease, they did not consider them as alone concerned. The former, holding that acridity or viscosity of the humours shared in the production of disease, prescribed medicines with the view of rendering them less viscid; the latter, though attributing disease chiefly to excessive or defective contraction of the solid tissues (spasm or atony), nevertheless prescribed alteratives for the humours, and evacuants for defective excretions. Stahl, on the other hand, was led by his animistic views to deny the efficacy of medicine almost entirely: he even threw doubt on the use of opium and cinchona bark. Though all these eminent men, and many others, added something to the general fund of knowledge concerning therapeutics, the treatment of disease by drugs improved but slowly, and was dominated by strange conceits and superstitions.

Scorpions, earthworms, woodlice and viper's flesh, also the excrement of the dog, goose, horse and pigeon, appear in the Pharmacopœia of the Royal College of Physicians of London of 1721. The formulæ were somewhat less complex than in the previous century; but one, "Mithradatium," contains 49 ingredients; another, "Theriaca Andromachi," 63, including viper's flesh; and one of the Confectiones, 50, amongst which appear bezoars, corals, pearls, and the flesh, liver and heart of the viper.

Amongst the drugs which appear for the first time are the following: — Canella alba, tartar emetic, secale cornutum, stramonium, gamboge, ipecacuanha and senega. Chemical knowledge has not reached the physicians, for the minerals are still divided into sulphurs, salts and earths; arsenious acid being included among the sulphurs. Twenty-five years later the Pharmacopœia of the College of Physicians indicates a considerable change. The compounds are much simpler, and with a few exceptions they are not unlike those of the present day in the number of their ingredients.

The Mithradatium, however, still contains 46 ingredients, and the Theriaca Andromachi 62. The long list of animal substances has disappeared, but a few extraordinary materials are still met with: crab's claws, the so-called "crab's eyes," viper's flesh (in an ointment), bezoars, woodlice and red coral are still official. On the other hand some useful remedies seem to have dropped out. Nux vomica, digitalis, senega, hyoscyamus, stramonium, male fern, and secale cornutum are no longer official. Spirit of nitrous ether is official for the first time. A large number of useful oils are introduced, and the chemistry is much more advanced.

During the latter half of the eighteenth century very great advances were made in all the sciences bearing on medicine. Haller founded Physiology. Chemistry had advanced greatly. Barthez, in France, advanced a more tenable vitalistic theory of the nature of disease, and Cullen's Materia Medica was in every respect a great advance on any which had preceded it. The London *Pharmacopœia*, published in 1788, and that of Edinburgh, which appeared in 1780, reflected the rapid

advance of knowledge in Physiology, Pathology, Chemistry and Medicine which now occurred. The excessively complicated formulæ, which the older Pharmacopœias contained, were swept away. The numerous absurd animal substances present in previous Pharmacopœias were almost entirely omitted. Digitalis, senega and male fern recovered their place in the London Pharmacopœia; and cascarilla, kino, calumba and quassia were introduced.

The last years of the eighteenth and the first years of the present century were marked by a fresh outbreak of theories concerning the cause and cure of disease which had, for the time being, a considerable influence on the treatment of disease by drugs.

Brown, a pupil of Cullen, maintained that the tissues of the body possess excitability; that life is the outcome of the action of stimuli, such as warmth, food, etc., on this excitability, which is uniformly diffused in all tissues; that sthenic diseases are due to excessive, and asthenic to defective excitement. All remedies are stimuli, and only differ in their power. Strong stimuli, such as opium, musk, ammonia and camphor, are useful in asthenic diseases; but, if given in excess, they may, by producing over-excitement, lead to debility: other substances, such as purgatives, emetics, etc., produce less excitement than is requisite for health, and are antisthenic, or debilitating. Brown held that, for the most part, diseases are asthenic, and his treatment therefore consisted chiefly in the exhibition of stimulants. He looked upon sthenic and asthenic conditions as affecting the entire economy, and took little note of local changes, holding that excitability is uniformly diffused; and that it cannot be augmented in one part only, for then it would be unevenly distributed. This doctrine was largely accepted, and modifications of it were promulgated both in Italy and in France.

Rasori held views not unlike those of Brown. Broussais also taught that life is due to stimulation; that to live is nothing else than to be excited: but, he considered that different diseases possess different degrees of excitability; and further, that as the sum total of excitability in the body is always the same, augmentation in the one part occasions diminution elsewhere. He looked upon all medicines as either stimulants or debilitants, but strongly upheld the view that all so-called general diseases have a local origin. Fevers, for instance, he believed to depend on gastro-intestinal inflammation. He classified medicines as debilitants, direct stimulants, and revulsives; and, like Rasori, he looked upon undue irritation as the cause of most diseases; practically, he recommended only debilitating agents in the treatment of disease. The English, Italian and French systems had, during the first two or three decades of the nineteenth century, great influence in determining the use of drugs, and the doctrine of Broussais affected treatment until after the middle of this century. But with increasing knowledge of Chemistry, Physiology and Pharmacology, belief in the Brunonian and allied systems gradually declined.

The last theory of disease and its cure which I shall notice is that of

Hahnemann, who, at the end of the last century, made the theory that "like cures like" the central point of a new system of therapeutics. Hippocrates pointed out the occasional value of similars, that is, of drugs which produce symptoms similar to those observed in the disease for which they are given; so, too, did Galen, and some later writers. But Hahnemann was the first who raised the proposition that like cures like into a natural law; and he conjoined with this view a belief in the power of infinitesimal doses. He formulated new theories to account for disease and the curative action of his drugs. He held that a spiritual power (the vital force) animates the human body, and that disease consists in a diversion of the automatic vital force into an abnormal direction. Drugs rightly selected can produce, in his opinion, a disease like to, but stronger than that for which they are given, and such medicinal diseases are more easily overcome by the spiritual or vital force than natural diseases. In selecting a drug for any particular ailment, it is therefore necessary to choose one which produces symptoms like to those which are present in the natural disease for which it is given. He said that knowledge of pathology, or of the causation of disease, is useless. The powerful action of infinitesimal doses he attributed to the fact that in their preparation succussion and trituration were much used, and these processes in his belief increased enormously the spiritual or dynamic power of the drug.

The theories of Hahnemann on the nature of disease and drug action have long died out; but there are still a few believers in the so-called law of "similars," and in the efficacy of drugs given in infinitesimal doses.

With Brown, Broussais and Hahnemann, another phase in the history of drug treatment closed. With them the theoretical systems of treatment, which had succeeded one another since the sixteenth century, came to an end. Therapeutics became rational. A tendency in this direction had long been manifest; with the increasing knowledge of Chemistry, Anatomy and Physiology during the seventeenth and eighteenth centuries, truer conceptions of the causes of diseases became more general; and it came to pass that drugs were increasingly used for the removal of causes apart from belief in any abstract generalisations. Alkalies were given for acidity, even though chemical theories of disease were discarded. The knowledge that the bronchial tubes are surrounded by muscle led to the tentative administration in asthma of substances such as opium and ether, without relation to any theories; and the good effects observed from evacuants in many ailments led to their extended use, without any definite regard to Sydenham's theory of aiding nature.

Morgagni's great work on *Pathological Anatomy*, published in 1795, threw a flood of light on the conditions of disease, and Bichat not only pointed out the importance of considering changes of tissues, as well as of organs, but urged that the true use of medicine is to restore organs and tissues to a normal state; and, by the discovery of the influence which drugs have on tissues and organs and the functions they subserve, the

way was cleared for the next great step in therapeutic progress. The advances of chemistry gave facilities, previously wanting, for exact investigation of the action of drugs. Stoerk, indeed, in 1762, had published a good account of the action of henbane, aconite, and some other drugs on the healthy organism, together with the therapeutic inferences he drew from this action; we find, however, few records of similar investigations, and at the end of the eighteenth century very little had been ascertained as to the exact manner in which drugs influence the body, or as to those constituents of drugs on which their properties are now known to depend. The progress of chemistry had indeed led to a search for active principles in vegetable substances; but Cullen (in 1778) threw doubt on the value of any attempts to determine them. In the early part of the nineteenth century, however, chemists were enabled to separate several important alkaloids. Morphia was discovered in 1816, quinine in 1820, strychnine in 1818. These discoveries facilitated those investigations into the action of drugs on the various organs and tissues of the body and their functions, of which Magendie was the pioneer, and have so largely influenced the therapeutic theories and practices of the present day. Magendie showed that it was possible to determine not only the organ on which a drug acts, but even the part of the organ. By a series of striking experiments he demonstrated that strychnine produces its tetanising effects not by influencing the nerves or muscles but by acting on the reflex centres of the spinal cord; and the methods by which he showed this have been more or less a model for all who have forwarded the work which he so ably initiated. Soon chemists throughout Europe were busy in attempting to separate the active principles from all the well-known drugs; and physiologists were equally active in trying to determine exactly the organs on which these principles act and the manner in which they affect them. Foremost among such workers was Claude Bernard, to whom, more than any man in this century, we are indebted for the progress made in the comprehension of the action of drugs; as, not only by his experiments on the physiological effects of many drugs, but also by his discovery of the part which the vaso-motor nerves and the muscular coat of the arteries play in the circulatory system, he prepared a way for the further investigations on the vascular system, which have led to the discovery of some of the most powerful means we possess for relieving suffering and saving life. His successors have been continuously occupied in following out the researches which Magendie initiated; and every year we see additions made to physiological and pharmacological knowledge, which, immediately or at some future time, will enable us to treat disease with increasing certainty. When it had been sufficiently demonstrated that substances derived from the mineral, vegetable and animal kingdoms have a specific effect on disease, and that this action in the case of animal and vegetable substances could be traced to the chemical compounds they contain, the method in which the structure of these compounds influences their effects became a subject of investigation. Blake in 1842 came to the conclusion

that all salts having the same base exert a similar action when introduced into the blood, and that a close relation exists between the chemical properties of substances and their physiological results.

We have now found that it is possible in many instances to form an idea, from the composition of a drug, of its influence on the body; that this influence may be altered in certain directions by modifying its chemical structure, and that new substances may be built up chemically to fulfil pharmacological and therapeutical requirements.

The advances of recent years have been chiefly in the direction of the discovery and production of new agents calculated to exercise definite pharmacological actions, of determining their exact influence, as well as that of the older drugs, on the various parts of the body and on the lower forms of life, of ascertaining the minute changes which take place in disease in the various organs, and of discovering the relation which exists between micro-organisms and the production of disease on the one hand and the products of the micro-organisms and the cure of disease on the other.

II. Present Principles of Drug Therapeutics

We give drugs in disease for two purposes: —

1. To restore health directly by removing the sum of the conditions which constitute disease. Here we act empirically, with no definite knowledge, — often indeed with little idea of the action of our drugs, but on the ground that in our hands or in those of others they have restored health in like cases.

2. To influence one or more of the several tissues and organs which are in an abnormal state, so as to restore them to or towards the normal; with the hope that if we succeed in our purpose recovery will take place. This purpose we effect by means of the influence which the chemical properties of drugs exert on the structure and functions of the several tissues and organs. Minute information, therefore, of the nature of the drugs and their action is essential for their proper employment.

Nature of Drugs. — Drugs were formerly looked upon as simple substances having, amongst other attributes, the power of curing disease, indeed the popular idea concerning them has not advanced beyond this view; but physicians now refer their influence to the textural and functional changes they are capable of effecting in definite portions of the body by virtue of their total composition, or that of certain chemical substances they contain. Not only do the elements of which a drug is constituted affect its action, but the way in which these elements are grouped and combined is of importance.

The effect which several of the elements exert in their compounds have been traced by Brunton, Ringer, Harnack, Binz and others. It has been shown that chlorine and bromine, potash, lime, and many other metals, always tend to act on certain tissues in a definite manner, unless their influence be neutralised by other elements with which they

are in combination. It has been shown also that small groups of elements may play a similar part in more complex compounds, that the action of NH_2 and NO_2, for example, can be as distinctly traced in the compounds in which they occur as that of chlorine or potassium or calcium. A compound containing the group NH_2 stimulates the medulla; a drug containing the group NO_2 acts on the vessels and dilates them.

On the other hand, in many of the organic compounds we are quite unable to trace the effects of the several elements; and it is rather the manner of grouping of the elements which seems to confer on the compounds their pharmacological and other properties. Two compounds may contain exactly the same elements and the same number of atoms of each, yet if these atoms be differently arranged the compounds may differ entirely in pharmacological and other properties. Methyl nitrite, and nitro-methane have the same formula ($CH_3 NO_2$), but the oxygen and nitrogen atoms in the two substances are joined together in a different way. The result is they act quite differently: the nitrite dilates the vessels; nitro-methane has no such action.

In the more complex organic compounds the addition or removal of one of these small groups of elements often greatly alters the pharmacological effect. Fraser and Crum-Brown showed many years ago that by replacing an atom of hydrogen in conine by one of methyl (CH_3) a great change in properties was effected. Conine paralyses the nerve endings alone, the methyl compound depresses the spinal cord. It is not always possible to anticipate the influence which the addition or subtraction of one or more of these groups will have on complex compounds which, like the alkaloids, are made up of a very large number of simpler groups. The result doubtless depends on the place which the added group takes amongst the other groups, or the effect produced by the subtraction on the arrangement of the other groups. Though the character and arrangement of the groups in a compound do not certainly indicate the action, yet they often give a good clue to it; they point to the manner in which the compound breaks up when taken into the system, and suggest the new combinations which may be formed. Again, they often indicate modifications and additions by which new compounds may be produced for the fulfilment of needs. Thus, for example, by adding the group NH_2, H.CO to the group $C.Cl_3$, COH (chloral) we get a compound chloralamide ($C.Cl_3$, CHO, HCO, NH_2) which has the soporific properties of chloral, but does not so deleteriously affect the cardiac and respiratory system. By the substitution in sulphonal of a molecule of ethyl (C_2H_5) for a molecule of methyl, trional is formed, which appears to have in some cases a better effect than sulphonal. Many of the modern remedies are the outcome of a knowledge of the influence exerted by various groups, and by the manner of arrangement of such groups in a compound.

In the laboratory we can easily so modify the composition of medicinal agents as to transform them into compounds having very different pharmacological effects.

If morphia (C_{17}, H_{18}, NO_2 (OH)) be boiled under pressure with water acidulated with hydrochloric acid, it loses a molecule of H_2O, and is converted into apomorphia (C_{17}, H_{17}, NO_2). If it be heated with soda and methyl iodide, codeia (C_{17}, H_{18}, NO_2, OCH_3) is formed. Pilocarpine, when heated with dilute hydrochloric acid, is converted into jaborine, a compound allied chemically to pilocarpine, but resembling atropine in its pharmacological effects.

The changes which can thus be effected in a drug outside the body may also be produced within the body; moreover these changes may vary with the conditions of the body. It is important, therefore, to determine the changes which can occur in chemical compounds under varying circumstances.

In drugs derived from the mineral kingdom the grouping of the elements is simple; the influence of the drug often depends almost entirely on one of the elements present — as, for example, in the compounds of iron and mercury — and we can easily comprehend all the possible alterations which such drugs may undergo in the system.

In the case of organic compounds belonging to the fatty and aromatic series, again, we may sometimes trace out the nature of the decomposition which goes on in the body, and estimate the effect of any new compounds which may be formed; but when we administer very complex substances, like the alkaloids, it is often impossible in the present state of knowledge to determine what changes, if any, take place; we cannot know, therefore, the nature of the effects which may be produced.

Still more difficult is it to determine definitely the action of crude vegetable drugs, the effects of which are due to the alkaloids, glucosides, oils, etc., which they contain. In many instances more than one of these active principles are present, and not unfrequently we find these closely related chemically, being probably derived one from another in the chemical processes going on in the plant.

The number of active principles in a plant is largely influenced by the circumstances connected with its growth, such as temperature, nature of soil, and so forth. Stenhouse found that broom grown in the sun contains four times as much alkaloid as that grown in the shade. Not only so, but the relative amounts of the various active principles will vary somewhat as the conditions under which the plant is grown are favourable to the occurrence of chemical changes, or the reverse.

From all these causes the effects of crude vegetable drugs, and therefore of the galenical preparations obtained from them, are apt to vary; and this variation is at times increased by differences in the method of preparation. Hence arises, perhaps, the divergence of opinions so often noted with regard to the therapeutic powers of certain drugs. The process of "standardisation" which has been already adopted in two instances in the British Pharmacopœia, and is likely to be extended, will to a certain extent obviate this source of error; for the standardised preparations will contain a uniform amount of the alkaloidal principles contained in a plant. But if the relative quantities of these principles vary under different con-

ditions of growth, the effects of preparations apparently identical will still be liable to corresponding variation; this may occur especially where drugs contain substances easily modified, as in the case of atropine and hyoscyamine. Ladenberg has given reasons for believing that the latter is changed into the former even by the process of extracting the alkaloid. Examples of such readiness to change, however, must be rare.

Notwithstanding all these possible sources of error the action of drugs on the system is moderately constant; but not until we are much better acquainted than we now are with the chemical nature of drugs shall we be able to explain the very diverse therapeutic results which are recorded.

The Nature of Pharmacological Action. — By the word "pharmacological action" is meant the action of remedial agents on tissues and the function they subserve in health and disease.[1]

The ultimate nature of the influence which drugs exercise on organised material cannot be absolutely determined; but, as Schmiedeberg has said, it must be chemical — using the word chemical in a broad sense.

When a pharmacological agent comes in contact with a tissue its effects may be purely chemical; it may act in virtue of its acid or alkaline properties, or by leading to decomposition of a purely chemical nature. It may also effect changes in the tissues by coagulating the albuminous or gelatinous materials contained in them; but, beyond this, it may alter their functions and vitality, without, so far as we can tell, producing chemical change in the strict sense of the term. When, for example, we pass through the muscle of a frog a very dilute solution of barium chloride, or expose it to a similar solution, the function of the muscle is distinctly modified, as shown by its increased contraction to stimuli, and by the prolonged duration of the contraction. By acting on the muscle of the heart or the vessel walls, their functions and vitality may also be altered; the systole of the heart is strengthened and prolonged, and the vessel walls are contracted. But if, after producing these effects on voluntary muscle, heart or vessel, we take means to wash the tissues through with a nutrient fluid containing no poison, the muscles and organs will resume their normal functions. We can, moreover, antagonise the effect of chloride of barium by means of a weak solution of potash, or by a solution containing NO_2, combined with a comparatively inactive base (sodium). In the latter case, however, NO_2, though neutralising the modification effected by barium on the function of the muscle, joins with it in depressing vitality, and the muscle quickly

[1] The word pharmacology was formerly applied to the consideration of medicines generally, including their physical characteristics and mode of preparation; and in this sense it is still often used in other countries. In England it signifies that department of therapeutics which concerns the effect of remedies as distinguished from their therapeutic application. It is well that the term "pharmacology" should be taken as including the action of drugs on morbid as well as on healthy tissues; otherwise it would be synonymous with physiological action, and we should have no term applicable to the investigations of the action of drugs on morbid tissues.

dies. A minute quantity of calcium chloride, on the other hand, whilst affecting the contractility of muscle, tends to prolong vitality. Now in these cases there is no evidence that any chemical change takes place; the influence is apparently molecular rather than chemical, for if positive chemical change took place it is not probable that the effects could be so easily abolished, either by the removal of the barium, or by the addition of substances between which and the barium chloride no chemical change takes place. The exact process by which the molecule of the drug acts on the ultimate elements of the muscle fibre in order to produce change in function is beyond our knowledge. It seems probable that the influence of chemical compounds on the muscular, nervous, and all other tissues of the body, is similar to that which occurs in the skeletal muscles or heart removed from the body. The functions of the tissues are altered by the influence which the molecules of the chemical compounds exert upon them, and their vitality raised or depressed. It is in this way that strychnine and physostigmine respectively stimulate and depress the spinal cord, that curare paralyses the nerve endings, that atropine paralyses the vagus endings and centre, and that the tissues engaged in secretion or excretion are stimulated or depressed. Most substances at first increase and then decrease the functional activity of muscle; in some the stimulating, in others the depressing effect is more marked: in some substances, indeed, no primary stimulating effect is observed. The same is the case with regard to the action of drugs on the other tissues within the body. Remedial agents for the most part first stimulate and then depress the functional activity of the parts they influence; but the stimulation may be more marked than the depressing effect, or vice versa; or it may be entirely absent.

The effect in all cases may be looked upon as "molecular," that is, it may be produced without ascertainable chemical or structural change. If the supply of the chemical compound in the blood cease, it is sooner or later washed out of the tissue by the circulating fluid, and the normal function is restored. In experiments on muscle tissue it can be shown that some substances, such as the nitrites which powerfully alter functional activity and vitality, can be easily washed out, and the muscle thus restored to its normal condition. Other substances, such as barium, are washed out with difficulty. It is probable that there is a similar difference in the influence of drugs on all tissues, and that this in part accounts for the well-known difference in the duration of the action of medicines. The removal of a drug from the tissues which it has temporarily influenced, unless the effect have been very strong, is followed by a return to the normal state; but it seems probable that under some conditions the continued interference with the function of a part is followed by nutritional changes of a permanent character. It is from this cause probably that alcohol in time leads to those changes in muscle and nerve which are characteristic of its prolonged imbibition.

In order that drugs taken by the mouth may act on various parts of the body, such as the spinal cord, brain and nerve endings, it is evident

they must be absorbed and carried by the blood to these several parts. The absorption of active principles no one now questions, though in earlier days it was denied. Cullen held that medicines act almost entirely by the influence they exert on the mucous membrane of the stomach and intestines; and in the first decades of the present century the necessity for the absorption of a drug antecedent to its action was doubted by many. Drugs carried by the blood do not affect the tissues equally: one exercises its influence on the tissues of the cord, another on those of the cerebrum, a third on the respiratory centre, and so on. To explain this we must assume that tissues have a selective affinity, and that, as the blood circulates through them, each retains or submits to the material which is in functional relation to itself.

Perhaps the most difficult part of pharmacological action to determine is the influence of remedial agents on the blood and nutritional processes. There can be no doubt that some agents markedly affect the hæmoglobin in the corpuscles, as shown by the cyanosis they produce; others, like chlorate of potash, are under certain conditions capable of causing dissolution of corpuscles, and there can be little doubt that the alkalinity of the plasma may be increased or decreased. But over and above these effects it would seem as if some substances, such as alcohol and arsenic, are capable of modifying the metabolic changes — delaying or accelerating them; but whether such results are due to a primary alteration in the blood, or to a direct influence of the alcoholic molecule on the tissues, is not known.

Besides influencing the functions of tissues in the manner which has been distinguished as molecular, drugs may produce direct structural changes in tissues. Apart from all chemical action, they may excite irritation and inflammation such as that which is produced by mechanical agencies. In this way they may produce important effects not only on the tissues with which they come in contact, but also on parts remote from them. By the irritation produced in the nerve endings in the tissue a centre with which these nerves are connected may be altered, and other tissues supplied by this centre may have their function and vitality increased or decreased. The vomiting produced by emetics, and the nutritional changes which occasionally seem to follow external applications, may be thus explained.

The influence of pharmacological agents under the abnormal conditions present in disease is by no means always the same as in health; the difference is, however, usually quantitative rather than qualitative. A weak walled heart, for example, is much more easily influenced by digitalis than a healthy one. The functions of the kidney can never be affected in health as at times they may be in certain diseases. Antipyretics exert, on those parts upon which they act, a different effect in a febrile as compared with a normal condition. Lastly, mercury and iodide of potassium have special action on certain forms of diseased tissue which we do not see in health. This is probably due to the fact that in the diseased conditions they act upon new tissue of a less stable character

than normal tissue; or it may be that new compounds are formed with the mercury or iodide which are easily broken up and destroyed.

As already pointed out, the pharmacological action of a drug is apt to be influenced by changes which the chemical processes of the body effect in the drug itself. Such changes may occur in the gastro-intestinal canal, in the blood, in the tissues, or at the moment of excretion. Hence the chemical composition of a drug is not unfrequently the key to its pharmacological action.

Principles on which Drugs are Selected. — *Rational Therapeutics.* — When a case of disease presents itself for treatment the first step is to determine whether any drug be known which has cured an exactly similar case. This can only be done, of course, when full knowledge of the clinical features and pathology of the case has been obtained. If no such drug is known one of two plans is adopted: we may select a remedy on the ground of analogy, because it has done good in an instance so like the present one that it may reasonably be expected to be again of service. If experience and analogy fail recourse must be had to such pharmacological knowledge as we may possess; that is, we may select a drug capable, directly or indirectly, of causing the return of one of the abnormal tissues and organs to a normal state.

Whether a drug be selected in the first place on analogical or on pharmacological grounds will largely depend on the bent of the observer. Some see analogies quickly, others more readily resort to reasoning. The same treatment may result from either attitude of mind.

The chief point in which the modern method of selecting a drug differs from that formerly employed is, that when empirical knowledge does not appear available we employ methods of reasoning founded more directly on the pathology of the disease and on drug action, instead of on metaphysical or fanciful theories as to the nature of disease and of remedies. Nevertheless, it must be pointed out that in the application of pharmacological knowledge to the cure of disease we still use hypotheses; and on the correctness of these our results must depend. The pathological changes in every ailment are more or less complex and wide-spread; the immediate influence of remedial agents is more limited: hence when we desire to restore health by urging the tissues and organs towards the normal state we have to make choice of the pathological condition which shall first be dealt with: and this we do in accordance with certain imperfect inductions to which experience has led us. We assume in each case either (1) that in diseased conditions there is naturally a return to health, or (2) that if the apparent cause of the ailment be removed cure will follow, or (3) that by the restoration of tissues and organs, which are the special seat of pathological changes, to their normal textural and functional state, or to a state approaching the normal, we promote cure; and further, that when organs are caused by drugs to resume their normal function, their improved condition may continue even when the drug is withdrawn.

The first assumption is one on which Hippocrates and Sydenham relied, and it lies at the root of much of our therapeutic reasoning. Experience proves to us that many diseases tend to terminate in recovery; but that, nevertheless, pathological changes at times occur in their course which, unless prevented by suitable remedies, will terminate life. Yet we often fail to save life by dealing with sudden causes of danger. The removal of the apparent cause, or of the more marked pathological conditions in a disease, does not always lead to a favourable termination. Each of these generalisations, however, holds good in a large number of cases; and in selecting a drug apart from the teachings of experience we found our judgment on our pathological and clinical knowledge; we decide under which of these generalisations the case before us falls, and then with the aid of pharmacological knowledge we select a drug to fulfil one of the following indications — a drug which will (*a*) so influence some organ or organs as to avert the tendency to death, (*b*) remove the apparent cause of the ailment, (*c*) restore as far as possible the tissues and organs, which are the special seat of pathological changes, to a normal state. In addition to these indications we are manifestly called upon to (*d*) relieve pain and suffering.

Our success will depend on the correctness of our judgment as to whether the case really comes under the generalisation we employ, and on the correctness of our pharmacological knowledge.

It is apparent that in one sense indication *c* includes *a* and *b*. In averting death or removing the apparent cause, however, we do not necessarily deal with the special seat of pathological change. We always meet indication *a* at once, and then indication *b* if we can.

Experience and Analogy. — The cases in which experience founded on simple observation can be trusted in the selection of a drug are few. The same collocation of symptoms and conditions are rarely repeated; yet, unless they are, when we select a drug on the ground that it has before done good, we act on analogy rather than on actual experience. In times past the judgments formed on the ground of experience of the action of medicines were very fallacious; to this the enormous number of medicines then used and now discarded are witnesses. Yet the discovery of mercury, quinine, arsenic, and many other remedies, is an evidence of the value of simple observation. Want of knowledge of the natural history of disease, of pathology and of pharmacology, is the cause of the errors which are made when experience is trusted alone.

Belief in a drug of no value is easily engendered if the natural course of disease be unknown; defect of pathological knowledge and observation leads rather to the misapplication of useful remedies. Quinine rarely fails in ague; but in a counterfeit of ague, say in the fever caused by suppuration in the liver due to gall stones, it is useless.

Pharmacological knowledge corrects many of the errors to which simple experience is apt to lead; the want of it permits their continuance. If a drug have no active properties it is surely devoid of medicinal effect unless it be a food; for medicinal action is the outcome of the

effects of active principles on tissues. It is always possible that in any particular drug the active medicinal agent may have escaped notice; but in the present state of chemical science it is not likely that undiscovered principles reside in such substances as sarsaparilla and hemidesmus: yet these drugs are given on the testimony of experience, — a testimony no stronger than that which has supported scores of other agents eventually discarded. If the indications given by the pharmacological examination of a drug are opposed to experience in its favour, the latter must almost certainly be at fault.

Experience and analogy, then, should only be trusted within narrow limits; but when we can combine the indications of experience with those of pharmacology we strengthen both. The influence, for example, of antimony in eczema, especially when combined with magnesium sulphate, has often been vouched for on the ground of experience; but not more strongly than has been the case with scores of useless agents. It can be shown, however, that antimony does, in the frog, influence the epithelium very markedly, as does arsenic; and this, without proving its remedial value, distinctly adds to the probability that those observers are right who hold antimony to be useful in some forms of eczema.

The value of the antitoxins and of thyroid extract is vouched for by many careful observers. Pharmacological knowledge is certainly not opposed to the probability of their usefulness; it rather supports it. On the other hand, it has so far given no support to a number of new animal substances brought forward recently, many of them on analogical grounds founded on some error in observation. To the use of analogy in drug therapeutics we owe great advances, especially in early times — it has been a great inciter to experiment, and is so still. Guided by due knowledge of the course of disease and of pathology it leads to increased knowledge; but as used in times past it has burdened our Materia Medica with much rubbish, as recoveries following the use of substances suggested by analogy have been looked upon as cures. It was by false analogy that mercury came so much into use in inflammations. When mercury was found to influence so markedly the swellings and thickening occurring in syphilis, it was used by analogy in all the forms of inflammatory disease which cause swellings and thickenings. As many of these naturally subsided thereafter, mercury was thus credited with a curative power in inflammation. It would be going too far to say mercury has no influence in inflammatory changes. There are probably conditions in which it is of service, but the facts that it is now so little used, and that no apparent evil has followed its abandonment, indicate that the views formerly held, and apparently grounded on experience, were, to a large extent, erroneous; and that the employment of analogy may, in this instance, have been productive of evil.

(*a*) *Method of averting the Tendency to Death.* — We find not unfrequently in the progress of acute diseases, and sometimes under other circumstances, that death seems to be impending by the failure in function of one organ when the condition of the others is compatible with

continued life; and this even when in the organ affected there is no evidence of fatal structural change.

The cardiac and respiratory systems are most commonly those in which such failure takes place. Suddenly or gradually, during the course of many diseases, the condition of the pulse points to failing heart action which threatens life; or again the blood changes essential to the continuance of life are imperilled by failing powers of the respiratory centre, or by paroxysmal obstruction to the entrance of air into the lung. These things may happen even though the heart and lungs are not the seat of any considerable pathological changes.

In case of heart failure we may fulfil the indication of averting the tendency to death by giving drugs which (α) strengthen the power of the heart or (β) decrease the work it has to do.

(α) In selecting drugs to strengthen the heart the whole of their pharmacological properties must be borne in mind. Digitalis is one of the most effective agents we have for increasing the power of the heart's action, but it contracts the vessels and is long in acting. By contracting the vessels it is capable of doing harm in certain cases of heart failure, especially in gouty people with tendency to high arterial pressure; because of the slowness of its action (especially when taken by the mouth) it is often given in vain in cases where the heart's failure is urgent. On the other hand, where the heart's failure is gradual and the arterial pressure low, digitalis is called for. Strophanthus does not contract the vessels, and seems to act more quickly; whether it acts as powerfully as digitalis is a point on which we are not agreed. Strychnine, as a heart stimulant, acts more rapidly than digitalis; when given subcutaneously its effects can often be noted in a few minutes; and, though perhaps they do not last so long as those of digitalis or strophanthus, they are more permanent than those of the volatile cardiac stimulants. Strychnine, moreover, has the advantage of being a respiratory as well as a cardiac stimulant: ammonia shares this advantage with strychnine, but it is more evanescent in its influence on the heart, although perhaps more immediate in its effects. The injection of ether subcutaneously is the most powerful means we have of immediately stimulating a failing heart, but its action is probably even more transitory than that of ammonia; though, owing to the fact that it can be injected subcutaneously, it is more frequently employed in urgent depression of the heart's power. The cardiac stimulation produced by smelling ammonia is of course of a reflex nature. Although ammonia has undoubtedly a stimulating effect on the heart, increasing both its force and frequency, it is not always easy to determine its utility in this direction. It is possible the condition of the stomach at the moment influences its cardiac effects to some extent. So far as it is converted into chloride it can have little action on the heart, although the chloride may stimulate the respiratory centre.

(β) Of drugs which act by dilating the vessels, and thus relieving the heart in its work, there is one — amyl-nitrite — which dilates the vessels in about ten seconds, and is therefore applicable in the most urgent cases.

As its influence on the circulation, however, ceases in two or three minutes, this drug, though of great value in immediate exigencies, must not be relied on for continuous action.

Nitrite of sodium and nitro-glycerine exert a distinct influence in from two to four minutes, but their effects continue for two or three hours; they are therefore serviceable in cases where we want to relieve the heart's action for a considerable period, though useless where instant effect is required.

Vessel dilators are of special use in warding off evil where cardiac failure is not accompanied by vascular dilatation. In certain forms of cardiac degeneration it would appear as if periodic waves of increasing arterial contraction become a grave source of danger, and these may be well met by the quickly or by the more slowly acting vessel dilators according to circumstances.

It is possible in some cases to combine a cardiac stimulant with a vessel dilator; indeed the vessel dilators may have at first a slight stimulating effect on the heart, even if, in large doses, they eventually depress it, which, however, is not definitely proved. The combination of a nitrite with ether is thus often distinctly advantageous in the relief of cardiac failure.

Any lethal tendencies of drugs used in cases where life is in the balance must always be borne in mind. It can be shown by experiments on animals that a slight excess of digitalis over the amount required to stimulate the heart may cause an immediate and permanent cessation of the beat; and there is reason to believe that in some forms of cardiac degeneration digitalis is capable of stopping the heart's action suddenly. On the other hand, in certain other ailments, such as pneumonia and delirium tremens, it would appear that the heart can bear large quantities of digitalis without injury. Unlike digitalis, strychnine seems to have no lethal effect on the heart even when given in large medicinal doses; and we rarely see indications of the physiological effects of strychnine on the nervous system following their use. The powerful effects of the nitrites on the circulation make us cautious in the use of these agents, the more so since, as before said, they are capable of depressing the contractile power of the heart: it is worthy of note, however, that, considering the extent to which they have been used, grave evil has very rarely been attributed to them; this may be due to the fact that the molecular influence they exert on tissue is not so permanent as in the case of many other drugs: It has been shown that they can readily be washed out of muscle tissue, which then resumes its normal function.

In cases where life is immediately threatened by defective blood changes due to failure of the respiratory centre, or to paroxysmal obstruction to the entrance of air into the lung, we may in the first place administer substances which have a directly stimulant action on the respiratory centre; of these perhaps the most useful are ammonia and strychnine.

Belladonna has also a powerful effect on the centre; it has an influence,

too, in relaxing undue contraction of the muscles of the bronchial tubes if it occur. In using it, however, we must bear in mind its wide influence over many other systems of the body.

In paroxysmal obstruction to the entrance of air into the lung the nitrite will often be found of value; one or two drops of liquor trinitrini, or a drachm of a 3 per cent solution of nitrite of ethyl, or two grains of sodium nitrite, will very often remove perilous dyspnœa by relieving the spasm which interferes with the entrance of air into the bronchi.

Even when we cannot remove the causes which lead to defective aeration of the blood, we may sometimes temporarily neutralise their ill effects by the inhalation of oxygen. It is quite true that in most cases where oxygen is used no permanent good is effected; but it is very commonly employed where the causes which lead to defective aeration are continuous: as a means of removing temporary cyanotic conditions oxygen is distinctly useful.

The reduction of hyperpyrexia occurring in the course of acute diseases is another instance of the use of drugs in warding off a tendency to death; but here drugs are probably of less value than other means. If drugs are employed quinine is by far the best remedy for this purpose, but less than 10 grains is generally useless. The employment of antipyrine, antifebrin, or phenacetin is very questionable practice.

(*b*) *Removal of the apparent Cause of the Ailment.* — In the removal of remote causes of disease drug treatment takes but little part. A foreign body in the stomach or intestines may be the cause of the pathological conditions leading to colic, vomiting or diarrhœa; and we employ pharmacological knowledge in the selection of emetics or purgatives for their removal.

Micro-organisms, too, may be looked upon as the cause of a large number of ailments. Proof is yet wanting that we can destroy micro-organisms in the blood and tissues by so-called germicidal substances such as perchloride of mercury, the sulphites, carbolic acid, etc.; even on external surfaces and on mucous membranes, as in ringworm and diphtheria, these substances often fail to destroy them, though they are capable of checking their growth.

Most of the other conditions usually called "causes" of ailments are really abnormal conditions of tissues and organs giving rise to groups of symptoms. In the series of antecedents which constitute collectively the true cause of an ailment, we often stop in an arbitrary manner at one of them and call it the cause of the collocation of phenomena by which the disease is signified. Practically by the word cause is usually meant the most remote of the antecedents which it is in our power to influence by drugs; it is by no means always the most manifest.

In considering whether it be possible to remove an apparent cause we have first to decide whether it is really in action, next whether it goes far enough back in the chain of antecedents, and, lastly, how far drugs can influence it. A gumma may have been the direct cause of a hemiplegia; we may remove the cell deposit by mercury or iodide, but yet no im-

provement may take place, for further structural changes have occurred. The gumma may not still be the cause of the loss of power, although at first it was. Again, cerebral symptoms may be due to changes in the vessel walls and high arterial tension — the latter being the outcome of the products of imperfect metabolism, which in their turn may have originated in imperfect digestion. To treat the high tension will not suffice; it does not go far enough back in the order of events: we must treat the imperfect metabolism or the indigestion. Lastly, the limit of the action of drugs comes to be considered: in the case of gout, syphilis, and a few other ailments, we can definitely affect structural change by drugs; in most cases, however, our power to remove a cause by drugs ceases as soon as it consists of definite statical tissue change.

The indication to remove the cause might of course be included in the next one relating to the removal or diminution of the special pathological changes present; yet practically in selecting a drug we have always first in our mind this question of cause, and it often leads to the selection of an apparently subordinate lesion for treatment. In nothing is the judgment more exercised than in determining whether we shall deal with the remoter or with the more immediate or evident causes of the case before us. After all, however, the removal of a remote cause, like the removal of the immediate factors threatening death, is only an instance of the general statement that when empirical treatment fails or is not possible, we try to cure by restoring individual organs as far as possible to a normal condition.

(*c*) *Restoration of Tissues and Organs which are the Seat of Special Pathological Changes.* — The influence of drugs in restoring organs to their normal state depends, of course, on the tissue changes they are capable of effecting — using the word tissue changes in its widest sense to indicate changes which we cannot physically determine, as well as those we can. This tissue change, again, is the outcome of the action of elements or groups of elements in a drug on one or more areas of the body.

The general methods adopted when the blood is in an abnormal state may be mentioned first. In some cases we have evidence that the normal constituents of this fluid are defective; in others we have reason to believe that substances not ordinarily contained in it are present; or that some of the normal constituents may be present in excess. In the first place we may attempt directly to make up the deficiency. We do this when we give iron in anæmia; for recent evidence does not tend to support the views of Schmiedeberg, and some other observers, who have asserted that in the use of iron nothing is added to the blood, and that its effects are due to changes brought about by it in the intestines. Another example of adding a constituent wanting in the blood is seen in the administration of the thyroid gland; and bone marrow acts like iron, if indeed it have any effect at all. To remove abnormal substances present in the blood various means are adopted. If we have reason to suppose that the products of imperfect metabolism are present we may attempt to promote their excretion by the kidneys or bowels.

It is possible, though by no means proved, that such products are excreted by the bowels; it seems likely that saline diuretics may also help to remove them. Another, and often a more effective plan is to prevent absorption of the contents of the intestine in the upper part of the intestinal canal by means of saline purgatives, such as sulphate of soda and sulphate of magnesia; a third is to give drugs which are supposed to facilitate the burning up of the intermediate products of metabolism. Alkalies, for example, are sometimes used for this purpose.

There seems reason to think it possible in certain cases directly to antagonise and destroy the effects of some toxic matters which cause disease. This at least seems the way in which the newly-discovered antitoxins act. It is supposed, for example, that the diphtheria and tetanus antitoxins act directly on the toxins, annulling their noxious influence. May it not be, too, that quinine, and likewise mercury, respectively antagonise the poison of the plasmodium in ague and the unknown toxic agent which exists in the blood in syphilis?

The chief effects of disease on other tissues and their functions which may be influenced by drugs are connected with — (α) Inflammation and its results. (β) Other morbid processes which lead to cell growths. (γ) Increased or defective function with or without ascertained physical changes.

Though inflammation may be, on the whole, a protective process — the reaction against some injurious material as Metschnikoff thinks — yet, as he also points out, its local effect on tissues essential to life may be destructive [*vide* art. Inflammation]; drugs are therefore used to mitigate or limit it. External inflammations may be dealt with by local stimulants or local sedatives. In conjunctivitis, for example, very dilute solutions of zinc sulphate are applied to the inflamed surface, and manifestly tend to subdue the process. They are supposed to act by contracting the dilated vessels. It would seem at times as if substances, such as atropine and morphine which depress the functions of the sensitive nerve endings in tissues, have a beneficial effect in relieving external inflammation. Inflammatory processes in the gastro-intestinal canal may be affected in a similar manner. It seems probable that minute doses of irritants, such as ipecacuanha and iodine, may sometimes act in the stomach and intestines as very dilute solutions of sulphate of zinc act on an inflamed conjunctiva.

Furthermore, in the stomach and intestine we may affect inflammatory tissue favourably by altering its surroundings, by removing irritating material from the surface of the inflamed membrane, and perhaps by supplying an unirritating covering in the shape of bismuth. This supposition, however, to account for the good effects which bismuth undoubtedly produces in irritated conditions of the stomach and intestine is very doubtful. It is at least as probable that an extremely small amount of the bismuth, in contact with the mucous membrane, becomes decomposed, so that some soluble bismuth is formed, which, being at issue

irritant, acts as the zinc sulphate does on the conjunctiva. All inflammation of parts which can be reached directly by local applications are amenable to similar treatment. We can act, for example, on the inflamed mucous membrane of the bladder by sedatives, or by slightly stimulating and germicidal substances which are taken into the mouth, carried by the blood to the kidney, and there excreted, as, for example, buchu and copaiba. It is quite possible, too, we may be able to influence the lining membrane of the tubes of an inflamed kidney, but definite proof that we can do so with advantage has not yet been given. It must be borne in mind that the whole surface of the gastro-intestinal mucous membrane, from the fauces downwards, acts to some extent as an excreting surface; so that we may influence inflammatory processes therein by the excretion of substances previously absorbed. There is some reason to believe, for example, that the advantages of chlorate of potash in inflammation of the fauces are connected with its excretion by the mucous membrane, and are not entirely due to its local influence at the time it is swallowed.

What power have we of effecting inflammation of organs which cannot be reached directly, or through the processes of excretion? It was formerly held that in antimony, aconite, and calomel, we have substances which directly limit the inflammatory processes in tissues; but no proof of this has ever been brought forward, and belief in it is waning. It is probable that we have some power to act indirectly on inflammatory processes in the internal organs. We can increase secretion in the neighbourhood of an inflamed part, and we can alter the general tension of the vascular system. We can also modify the local vascular condition to a slight extent by dilating vessels in parts adjacent by means of pharmacological agents. In two other ways, also, it is possible by drugs indirectly to influence inflammatory processes in parts subjacent to cutaneous surfaces. There is evidence that cutaneous irritation has a distinct effect on the vascular supply and the nutrition in adjacent parts, and clinically it appears in some cases to limit inflammation. The other method is to give drugs which exercise a sedative influence on the mechanical conditions affecting the part inflamed. It is thus that opium is used in peritonitis.

The products of ordinary inflammation which interfere with the functions of tissues may possibly, when consisting of cell growths, be broken up and absorbed under the influence of mercury and iodide of potassium, as the products of syphilitic inflammation certainly are. We have as yet no strong proof of this, though analogy has led to an extensive use of both substances for the removal of the various forms of inflammation; and the disappearance of deposit has so frequently followed the use of these drugs that we can hardly doubt that some useful effect is produced. There is reason to believe also that we can cause the absorption of inflammatory deposits by stimulating the nerve endings in adjacent areas. As a rule, for this purpose, preparations containing mercury or iodine are employed, often with friction. It is a moot point whether the dissipation of inflammatory deposits which certainly appears

to take place under these applications is due directly to the absorption of these substances, or indirectly to their stimulating action on the cutaneous surface. Though mercury will pass through the skin, we have no proof that either iodide of potassium or iodide of lead do so: nevertheless they are manifestly of service at times. On the other hand, the irritation they cause is so slight that we can hardly attribute to this agency the absorptive influence these applications seem to possess.

Concerning the removal of other cell growths which interfere with the functions of tissues we have but little information. In all ailments which have any resemblance to the granulation tissues of syphilitic deposits we use mercury and iodine, and not unfrequently we see absorption take place; but we do not at present know the natural history of such ailments sufficiently well to feel assured that the disappearance is due to the drug. Arsenic can be shown to have a very decided effect on the nutrition of the skin, and it sometimes distinctly influences inflammatory deposits therein. It is supposed also to exert some influence on sarcomatous and cancerous tissues, but here again more exact observation is required.

Drugs such as chloral, belladonna, physostigma, and nux vomica, act on the tissues of certain parts of the brain and spinal cord, and thereby increase or decrease the functions of those parts. We can depress the functions of the motor nerve endings with conine, and the sensory nerve endings with aconite. We can paralyse the involuntary muscle fibres directly with the nitrites, or indirectly by chloral hydrate, which depresses the functions of the vaso-motor centre. We can stimulate or depress the functions of the cardiac muscle. The tissues of the various glands may likewise be stimulated or depressed. We can improve the nutrition, and therefore the function of almost all the tissues, by iron, cod liver oil and lime; and indirectly we can produce the same effect by the gastric tonics and digestives which promote the taking and absorption of food.

Our knowledge of the method in which drugs influence tissues in health and disease is largely, of course, the outcome of observations made on the effects of drugs on the functions which they modify; we must discriminate, however, between the action of drugs on an organ as a whole, and the changes in function which arise from drug influence on one of its tissues or on one of its parts. In restoring the function of an organ we have then to consider the influence of the drug on the various tissues and parts of which it is composed. In dealing with the cerebral functions, for example, the effect of the remedy on vessels as well as on cerebral tissues has to be remembered; and in the restoration of the cardiac functions the effect of agents on various portions of the nervous system as well as on the muscle should be borne in mind. The influence, too, of changes in one organ on the functions of another are very considerable, and it is often by acting on a healthy organ by stimulating or depressing its functions that we are able to restore another from a pathological to the normal condition.

In a case of cerebral hæmorrhage, for example, in which the brain is the main seat of pathological change, we know of no drugs which by directly influencing its tissues will bring about its return to a normal state. We are able, however, to act upon it indirectly by purgatives which tend to lower blood pressure, and after a while by giving drugs which improve the general nutrition. In valvular affections of the heart we cannot remove the chief pathological condition, but by acting on the cardiac muscle and its ganglia we can so strengthen and moderate the beat as practically to restore its normal function.

In phthisis we have hardly any power to influence lung tissue directly: but, by substances such as cod liver oil and lime which improve the general nutrition of the body, we can indirectly, perhaps indeed to some extent directly, help to restore the lung tissue and function. In bronchitis we can act directly on the tissue of the mucous membrane, and promote its normal secretions; but in pneumonia we probably cannot influence the affected tissues directly, although we employ salines with a vague idea that we may do so. Here we are limited in our action to sustaining the functions of other parts, in which the pathological change is much less marked, until such time as resolution may take place. It is possible, indeed, that expectorants sometimes influence the lung changes favourably by promoting secretion from the bronchial mucous membrane adjacent to the inflamed tissue; but it is unlikely that they act on this tissue itself. In pleurisy we are quite as helpless so far as direct drug treatment is concerned: we know no drug which has any direct effect in reducing pleural inflammation, and we are limited for the most part to the exhibition of agents for the relief of pain. Yet even here, when the acute stage has passed, we may promote the restoration of the pleura to a normal state by iron and nutrients.

Though we have no more power over peritoneal inflammation than we have over that occurring in the lungs or pleura we are able in peritonitis to give some aid by limiting the movements of the inflamed part. Opium probably influences the nerves supplying the intestinal muscles, and thus decreases peristaltic action. It also fulfils the next indication, the relief of pain. Here again, as in many other instances, in the efforts we make to restore parts pathologically affected we act on other and more or less normal structures. We have no reason to believe that the chief effect of opium, either in relieving pain or in checking peristalsis, is due to any large extent to its action on the nerve endings in the affected part.

In a few cases we attempt to restore the normal functions of an organ by the addition of certain materials which are lacking in its secretion. Thus, for example, in dyspepsia we administer pepsin; or we may aid duodenal digestion by a remedy derived from the pancreas; or we may give bile where we think this secretion defective. In all these cases, however, our immediate objects are in the first place to relieve discomfort, and in the second to restore the normal functions of the gastro-intestinal tract which are interfered with by the abnormal state of their contents due to the absence of pepsin, trypsin, and bile.

Sometimes we appear to apply pharmacological substances to influence a symptom rather than a pathological state, as when we use an antipyretic in fever. Here, however, we are really attempting to act on the pathological conditions causing high temperature; but not knowing what these are, we have to use a remedy in ignorance of the exact nature of its action.

In administering drugs to restore tissues and organs to a normal state we usually act on the supposition that an organ thus restored will maintain its improved condition even when the drug is withdrawn. When digitalis, for example, is given in cardiac dilatation and irregular action it is assumed, and for the most part rightly so, that if we can restore or partially restore the heart to a normal state it will so remain when the medicine is withheld. We do the same in bronchitis when we administer expectorants; in fact we apply a generalisation in this matter, as in many others, founded on a weak induction which must be referred to one or more inductions of wider scope. The reason that a tissue or organ restored to its normal state by a drug does not revert to its abnormal condition on the loss of the drug, depends partly upon the fact that every altered condition of an organ reacts on the surrounding tissues and organs; and partly on the tendency to revert towards the normal when perturbations have ceased to act.

(*d*) *Relief of Pain and Suffering.* — This indication has to be followed not only from considerations of humanity, but because pain and suffering, by their influence on nutritional processes, tend directly to prevent the return of tissues and organs to their normal state. The relief of pain may be accomplished by drugs which depress the functions of the sensory nerve endings, or act on certain parts of the central nervous system. The nerve endings may be affected through the circulation or directly. It is probable that most of those substances which depress the tissues of the central nervous system, those especially which are in relation to its higher functions, have also some influence on the nerve endings, though by no means in like proportion. On the other hand substances, such as cocaine, which very distinctly paralyse the sensory nerve endings, have comparatively little effect in preventing the perception of pain in the cerebrum. The influence of substances which act directly on nerve endings is practically much affected by the relations between themselves and the epidermis. The epidermic covering is probably a complete bar to the action of cocaine on the nerve endings; proof has not yet been given that, even by combining it with substances such as chloroform and lanolin which are said to aid the passages of drugs through the epidermis or its ducts, any effective influence is exerted on the tissues beneath. The epidermis likewise almost entirely resists the passage of morphia: hence opiate applications are far less frequently of benefit than is popularly supposed. On the other hand atropia, although not a powerful depressant of the functions of the nerve endings, passes readily through the epidermis; so too does aconitine, which has, however, in addition to its anæsthetic effects on the

nerve endings, an irritant effect on other tissues. Conium, like cocaine, has no action when applied to a surface covered with epidermis.

The exact part influenced by analgesics acting on the central nervous system is not known.

Substances which depress the higher cerebral functions such as anæsthetics, chloral, bromide of potassium, are undoubtedly analgesics; but opium, which stands first and foremost of all drugs in the relief of pain, may act as an analgesic without exerting the slightest recognisable influence on the higher centres. We have no evidence that its influence is largely due to its local action on the nerve endings; morphia will indeed relieve pain applied locally, but this may be due to its absorption into the blood. It certainly has no such depressing effects on the nerve endings as cocaine; if injected subcutaneously the place of injection is a matter of indifference. Possibly it influences the gray matter in the cord along which painful sensations are conveyed, and the continuation of the gray matter into the brain; or it may affect the centre for the reception of pain.

The exact point, then, on which morphia exerts its effect in producing analgesia is still unknown. Such too is the case with the newer analgesics — antipyrine, antifebrin, and phenacetin. They likewise influence painful sensations in a manner for which neither their local action nor their influence on the cerebrum can account.

In choosing an analgesic the pharmacological influences of the drug, other than those which effect the relief of pain, are not to be forgotten; these secondary actions often limit their use.

Not only must we relieve pain where possible, but all forms of suffering also; and next to pain insomnia is perhaps the most distressing of these forms. There is reason to believe the presence of certain elements and radicals in drugs gives them a power of depressing the tissues of the higher centres of the brain, and thus causing sleep. Almost all soporifics are derived from the fatty series, and many of them contain the elements chlorine and bromine. It seems probable that these elements, and also the fatty radicals, directly depress the function of the nerve cells in the cortex. The structure of hypnotics which do not belong to the fatty series, of which opium is the only one of importance, is not sufficiently known to enable us to ascertain to which of its constituent groups of molecules its effects are due. As in the case of analgesics the use of soporifics is limited by the extent of their other pharmacological effects; chloral depresses the cardiac and respiratory centres, the former to a dangerous extent when administered in large doses. In the newer compound chloralamide this effect is in part avoided by the presence of a molecule of formamide, which contains a group $N.H_2$ capable of stimulating the centres in the medulla. It still remains to be seen whether this is sufficient to neutralise entirely the depressing action of chloral.

Paraldehyde produces few special effects other than those procuring sleep, but its taste and the odour it gives to the breath are very objectionable; it is moreover much less certain in its effects than chloral. Sul-

phonal is also less certain than chloral; it is devoid of the unpleasantness of paraldehyde, but it seems at times to disturb muscular co-ordination, and it is said to lead to the presence of hæmatoporphorin in the urine.

III. Principles of Administration

In the administration of drugs the chief point for consideration is the method by which they can best be brought, in the requisite quantity, in contact with the tissues to be influenced.

Methods. — Drugs may be introduced into the body in many ways, which may thus be shortly enumerated.

1. *By the Skin.* — The skin presents two pathways for the absorption of drugs, viz., through the epidermis or through the cutaneous glands. Whether drugs actually penetrate the epidermis is very doubtful, and it is found that the more effectual ways of securing absorption through the skin are those which appear most apt to carry the drug into the interior of the cutaneous glands, such as the inunction of a mercurial ointment, the exposure of the skin to the hot moist vapour of a calomel fumigation, or the solution of the drug in chloroform as a liniment. By this mode of administration we avoid any disturbing influence of the drug on the digestive organs, and young children can thus easily be put under treatment. The disadvantages consist in uncertainty as to the quantity of drug absorbed, and in the unpleasantness of greasy and sometimes dirty applications to a large surface of skin.

The following means are usually adopted for securing cutaneous absorption: —

Fumigations Inunction of ointments or liniments Endermic applications to surfaces denuded of epidermis	Effectual.
Plasters continually applied Baths Medicated poultices and fomentations	Of doubtful value.

2. *By the Alimentary Canal.*

(*a*) By the stomach. The disadvantages of stomach administrations are —

(*α*) The drugs may be variously changed and decomposed by the digestive juice.
(*β*) They may disturb the digestive functions.
(*γ*) There is often delay in action, the rate of absorption being influenced by the solubility of the drug and the condition of the stomach mucous membrane; hence certain substances, such as sulphonal, are very uncertain in the time of their action.

(*b*) By the rectum in the form of enema and suppository. Absorption is slow from the rectum in the case of most drugs, and the dose

needed is larger than when given by the stomach. Strychnine and tobacco are exceptions to this rule.

3. *By the Respiratory Mucous Membrane.* — This is probably the most rapid means of entrance for drugs, owing to the large absorbent surface of the lung, and to the fact that the blood into which the drug has passed goes directly to the heart. Hence the extremely rapid action of amyl-nitrite. This method of administration is limited, for the most part, in its application to drugs volatile at the temperatures of the body, but injections into the trachea have been made; atomisation and insufflation of powders are commonly employed in local medication of the respiratory mucous membrane.

4. *By the Genital Mucous Membrane.* — Absorption through this channel is slow and uncertain. Usually the injections, pessaries, bougies, etc., used in this form of medication are employed for their local effect only.

5. *By Hypodermic Injection.* — This has the advantage of directly introducing the drug into the lymph stream without any decomposition. The influence is rapid, and the dose of the drug can be accurately graduated. The use is limited to drugs which are not irritating, and, for the most part, to those of which the dose is small.

6. *By Intravenous Injection.* — This is practically only used for the introduction of large quantities of saline fluid, though ammonia has thus been given.

7. *By Intraserous Injection.* — This has been employed in exceptional cases, but, so far as drug treatment is concerned, is of no value. The rapidity, however, with which absorption from serous cavities takes place is of importance in other relations.

Dosage. — The dose of a drug is not a fixed quantity, but must be determined according to the purpose for which the drug is used, and the conditions under which it is used. The conditions which chiefly influence dosage are age, sex, size and weight, and disease.

Age. — The usual rule is to take the adult dose as 1 year, and make a fraction, which has the age of the child for a numerator, and this age plus 12 for a denominator: this gives the fraction of the adult dose which is suitable for the child. Thus, for a child of six the dose would be $\frac{6}{12+6}$ or one-third of the adult doses. This is, of course, a mere approximation; moreover, each drug has to be considered separately in this respect. Children, for example, bear much larger relative doses of belladonna and arsenic than adults; but of opium, on the other hand, smaller doses.

Sex. — Women differ considerably from men in their reaction to medicine; the dose for a woman is usually considered to be four-fifths of that for a man.

Size and Weight seem to have less influence than would be generally supposed. It is only in exceptional cases — that is, where the size and weight are very small — that these factors need be taken into consideration.

The Present Disease. — This has often an important bearing on the dose. Any ailment which interferes with the functional activity of eliminating organs may seriously modify drug action. Hence, in kidney diseases, for example, opium has at times an exaggerated action.

As the dose of a drug has to be adapted to the changes in the tissues and organs it is meant to affect, and as the tissues of similar kind in different individuals are not influenced by the same amount of a drug, the dose which will effect its purpose has often to be arrived at by experiment — that is to say, by gradually raising it until a definite result is obtained.

Circumstances modifying the Influence of Drugs. — *Idiosyncrasy.* — One or more of the tissues may be unduly susceptible or insusceptible to the action of a drug. It is well known that the smallest quantity of calomel will salivate some persons, and a very minute dose of quinine will cause a rash in others. The explanation of this is quite unknown, but even the simplest tissues vary in their reaction to drugs; the excised muscles of one frog, for example, may differ considerably in their ordinary reactions from those of a series of other frogs without any other ascertainable differences in the experiment. [*Vide* art. "Temperament."]

Toleration. — When, on taking a drug continuously, the first effects decrease until they are no longer noticed, toleration is said to be established. In some cases this may be due to conditions causing increased elimination, or to the initiation of new chemical changes by which the drug becomes altered and even rendered inert. It may, however, also be due to some modification in the reacting tissue, caused by the continuous contact of the drug. It would appear as if toleration can be established more readily with some drugs than others; with opium, for example, it is easily established. For arsenic the toleration is not so readily established, unless indeed we accept the stories of the Styrian peasants. For chloral hydrate tolerance seems to become only partially established; patients can become habituated to larger doses, yet at times toleration seems temporarily to disappear, and a large habitual dose may at last have a fatal effect.

The duration of action of a drug is likewise dependent on the rapidity of its excretion and its adhesion to the tissues. The difference between drugs in this matter is enormous. Such substances as ammonia, ether, the nitrites and alcohol, produce their effects on the tissues quickly, and their effect as quickly passes away. An ordinary dose of ammonia or ether acts within a second or two; its effects do not last more than half an hour or an hour. Two grains of nitrite of sodium begins to act in two or three minutes, and its influence cannot be detected after three hours. Digitalis, on the other hand, does not show any signs of affecting the system for a long time, but its effect is long continued. It is manifest that this difference in the duration of the action of medicines should be considered in our combinations of them. It seems probable, for example, that if ammonia and digitalis are given in combination the ammonia will have ceased to act before the digitalis begins.

Cumulative Action. — Some drugs are quickly excreted, others are stored up in the body, and may not exert their characteristic effect until a certain amount has accumulated. This is the case with digitalis, for example. When this drug is taken in small doses, its special effects are not seen, as a rule, for two or three days. Cumulative action of a drug is usually due in part to difficulty of excretion, but also to the stronger adhesion of its molecules to the tissues. Digitalis, as a matter of experiment, is washed out of tissues with much greater difficulty than many other substances. The reverse is the case with curare, which is so slowly absorbed from the stomach and so quickly removed from the tissues and excreted that, if the drug be taken by the mouth, a sufficient quantity does not abide in them to produce its characteristic effect. Hence it must be given subcutaneously.

Sources of Fallacy in Therapeutics. — Some of the fallacies arising from defective observation and other causes have already been pointed out incidentally.

One is the assumption of pharmacological knowledge which does not exist. Some knowledge of the action of drugs on various parts of the body has been obtained, but concerning the effects of a large number definite information is wanting. Unfortunately, when knowledge is wanting, suppositions founded not on experiment but on fancy or on imperfect observation usually take their place. The reputed action of many drugs as cholagogues, diaphoretics, diuretics, etc., is founded on the most slender basis; yet it is constantly alleged as if it were founded on real knowledge. Of the alleged diaphoretic action of such substances as sassafras, and serpentary, nothing certain is ascertained. Again, under what conditions the so-called "expectorants" produce their effects we do not know, and so forth; indeed the action of most drugs on the tissues and organs is guessed at rather than known. Yet in therapeutic reasoning these hazy apprehensions are usually accepted as a basis for treatment.

A second source of fallacy is the persistence of old and baseless theories. The opinions of Hippocrates and of Sydenham; those of Willis, concerning the aiding of nature with regard to fermentation; of Boerhaave, on obstruction of the vessels; of Brown on asthenia, still colour our therapeutic reasoning, and lingering like the nomenclature of their inventors, like it they influence thought.

Limits of the Utility of Drugs. — Drugs only act beneficially when they can exercise such influence on the morbid changes in tissues and organs as to restore the parts to a state compatible with systemic life. But in a large proportion of cases such restoration is impossible. Unfortunately for the reputation of drugs it is considered necessary to give them in all cases, even where it is manifest that the case is beyond the limits of drug treatment. The prevalent want of belief in drugs is largely due to the fact that they are expected to achieve the impossible.

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CLIMATE IN THE TREATMENT OF DISEASE

The Climate of a region or site is the combined effect of the atmosphere and of the nature of the surface in their relation to man. Of these the atmosphere, which is the product of many more or less varying agents, is the chief. The most important *qualities of the atmosphere* are: —

1. The chemical composition. 2. The organic and inorganic substances floating in it. 3. The temperature and its variations. 4. The degree of humidity. 5. The diathermancy. 6. The transparency and the quality of light. 7. The density and pressure. 8. The electrical conditions. 9. The circulation of the air — the directions and the force of the winds.

The *climatic character of a locality* depends chiefly: —

1. On the distance from the equator. 2. The elevation above the sea. 3. The relation of its position to adjacent seas or large inland lakes, or deserts, or marshes. 4. The predominating winds. 5. The nature of the soil: whether rock or dry porous ground, such as sand, allowing rapid percolation of moisture, and enclosing between the solid particles a large amount of air; or stiff, more or less impermeable ground, such as clay, peat, or marsh. 6. Configuration of surface: the amount of shelter, the position on a slope, terrace, or plateau, or in a valley; the aspect towards the sun, and possible amount of sunshine. 7. The mode of the cultivation of soil,

whether arable fields or pastures; the planting and clearing of forests; the density of population; the establishment of manufactures; the amount of drainage of the rural and the urban districts.

This article will be divided into three sections, as follows:—

First Section: Remarks on some of the principal elements of climate.

Second Section: Principal climatic regions and health resorts.

Third Section: Use of climate in the treatment and prevention of disease, with a sub-section on the use of "home" from a hygienic and therapeutic point of view.

First Section. — Remarks on some of the Principal Elements of Climate

1. *Composition of the Air.* — At one time it was generally maintained that the composition of the air was the same in all parts of the earth — at the tops of the mountains, on the sea, in rural and in town districts; but the researches of Tyndall, Frankland, R. Angus Smith, and others have shown that there are slight differences from the usually assumed composition, viz. —

Oxygen	. .	20·96
Nitrogen	. .	79·00
Carbonic acid	. .	0·04
	in	100·00 volumes of air.

Although the differences in the proportion of oxygen rarely exceed $\frac{1}{10}$ volume, such a plus or minus is of great importance if we consider the large quantity of air which we inhale, and if we may assume that any deficit is generally associated with the presence or the increase of more or less injurious substances.

R. Angus Smith found even in the same town considerable differences in the proportion of oxygen, *e.g.* in a northern suburb of London (Belsize Park) 21·01 per cent, in the middle of Hyde Park 21·005, in the Eastern district 20·86, in the tunnel of the Metropolitan Railway 20·70. In an open yard before a house more oxygen was found than within the rooms of the house. At the same spot he found differences under the influence of weather — more oxygen during and after rain than in dry and foggy weather.

Carbonic acid was first found by De Saussure as a regular constituent of the air in the proportion of 3·6 to 6 parts in 10,000; but its percentage varies considerably. Thus Angus Smith found in crowded law courts as much as 20, and in theatres even 32 in 10,000; and Pettenkofer found 20 to 58 in 10,000 in crowded schools at Munich. It is probable that air rich in carbonic acid is also rich in other impurities and in bacteria.

The air contains other gaseous substances, such as ozone, antozone, ammonia, on which we cannot enter here; and the vapour of water, which we shall discuss under humidity.

Very important are the solid substances floating in the air, the nature

of which varies considerably at different localities and under different conditions. They are partly inorganic, such as salty particles, silica, chalk, iron, etc.; partly organic, such as pollen, algæ, bacteria, fragments of hair, vegetable fibre, and insects. Some of these substances are innocent, or nearly so; others are injurious. Ehrenberg, Schwann and others directed attention to this matter long ago; but to Pasteur and Tyndall our debt is greatest. Pasteur has shown the absence of organic impurity on glaciers, and its presence in large quantities in villages not far distant.

The recognition by Lister of the influence of these suspended matters on wounds, and the adoption of successful means to exclude them, mark an epoch in the history of Medicine; and their presence in the air of different localities deserves attention in the appreciation of climates. On this depends the septic or aseptic character of the atmosphere; and the predominant feature of the localities most beneficial in the treatment of tubercular phthisis is the aseptic character of the atmosphere.

2. *Temperature* is a most powerful modifier of climates. We distinguish between radiant or sun heat, and shade or air heat. The rays of the sun have great power of heating the human body and other solid substances on which they fall, but heat only slightly the air through which they pass. The air would, in fact, allow the heat to pass through it entirely — it would be, to use a scientific term, quite diathermic — were it not for the watery vapour it contains. On the amount of this vapour depends the degree of the diathermancy of the air, which is a very important factor of different climates. The more vapour the air contains the less powerful is the direct or radiant sun heat.

The shade temperature is due mainly to the warmth imparted to the air from the ground — water as well as land — previously warmed by the sun's rays. The shade temperature may, however, be greatly influenced by currents of air from distant regions, viz., warm or cold winds.

Melloni and Tyndall discovered that the water vapour is much less diathermic to the invisible waves of heat radiated back from the earth than to the direct luminous rays of the sun. To this is due the protecting influence of the vapour on the ground, especially during the night — without it the greater part of the heat absorbed during the day would be rapidly radiated into space, which indeed does occur when the air is very dry and the sky cloudless.

The nature of the surface of the ground exercises great influence on the amount of heat which is absorbed and reflected. We can only briefly allude to Frankland's instructive experiments on this subject. The nearer the colour of the ground approaches to white (snow, chalk cliffs, white walls, etc.) the more the direct sun heat is reflected by it, the less heat is absorbed; the darker the ground (grass, green leaves) the less heat is reflected, the more is absorbed. The ground which absorbs more heat from the direct rays of the sun can give out more heat during the night and *vice versa*. The influence thus exercised on the climate of a place is evident, and the white snow fields of the Alps in winter form a well-known illustration.

We cannot enter on the distribution of temperature in the atmosphere on the surface of the earth, or on the great differences existing between the distances from the equator and the isothermal lines (with the same annual temperatures), and the isochimenal lines (with the same winter temperatures), and the isotheral lines (with the same summer temperatures). We must refer to Humboldt, Dove, Carpenter, Haughton, Scott, and others, for accounts of the warming influences of the equatorial currents of the sea, and of the chilling action of the Arctic and Antarctic streams. This and other factors of climate are very clearly described in the Lumleian lectures on "Aero-therapeutics" (1894) by Dr. C. T. Williams.

The temperature of the sea-coasts, however, is influenced not only by great sea currents; the nearness of oceans acts powerfully on the temperature of large tracts of continents — the range of temperature, as a rule, increasing from the coasts towards the interior. The Pacific, the Atlantic and other oceans diminish the annual range of temperature on adjacent shores to 20° F. and less; while in the interior of large continents — as in the centre and north of Asia — the range may be 60°, 80°, and even 100° F.

Mountains and high elevations above the sea act likewise to some degree as equalisers of temperature by lowering the annual range. In addition to this high mountain ranges act as shelters to the leeward regions; they condense the moisture on the side towards the sea, and render the air currents on the leeward side drier. We see this, for instance, by comparing the dry climates of Tibet and Cashmere with those of the windward side of the Himalayas, and those of the eastern side of the Rocky Mountains with those to the west of them.

Our knowledge of the influence of different degrees of temperature on the human body is still imperfect. Experiments have shown that cold acts as a stimulant and increases the amount of carbonic acid exhaled; but Pflüger has found a similar increase from heat, and Marcet came to the same result from his observations on the island of Teneriffe: we must infer, then, that heat, up to a certain limit, acts likewise as a stimulant. Our general views on the influence of temperature are based partly on the effects of different seasons on the health of individuals; partly on the effects of moving during winter to warmer climates, and *vice versa*; partly on the consideration of the physical and mental constitution of peoples dwelling in different regions: but the coexistence of other climatic factors — such as moisture, light, rarefaction, or condensation of air — render inferences difficult, a difficulty further increased by differences in the manner of life.

It is necessary to distinguish between radiated or sun heat and shade heat. We do not yet know how great a degree of sun heat can be borne. It is certain that sunstroke is very rare in great sun heat in the pure and comparatively dry air of high elevations; and this seems also to be the case on the ocean. High shade temperature is, however, much less easily borne, and persons who can do hard work in a sun heat

of 120° become rapidly exhausted in a shade heat of 90°. Here again we must bear in mind that we cannot distinguish the effects of temperature from those of moisture, electrical condition, and movement of air. Different individuals bear heat very differently; and many Europeans living in hot climates injure themselves by continuing to take the same kind and amount of food and stimulants as they do at home (Ranald Martin, Parkes, Fayrer, and others). However, as Parkes says, great heat in shade exerts "a depressing influence, lessening the great functions of digestion, respiration, sanguification, and, directly or indirectly, the formation and destruction of tissues."[1]

At climatic health resorts, however, we have not to deal with high, but with moderate degrees of heat, such as we find in summer in temperate, and in winter in hot climates, namely, between 55° and 70° F. In such temperatures the organism loses less heat than at lower degrees. In strong persons, after long exposure to such temperatures, we often find a certain degree of lassitude, diminution of appetite, and impairment of the functions of digestion, respiration, circulation, and metabolism. Weak persons, on the other hand, often exhibit greater energy of all the functions of the mind and body, gain in weight, and are less liable to disease. Hence the value of such climates to permanently delicate persons, or to those temporarily weakened by disease, and to the elderly.

The effects of low temperature are likewise rarely observed alone; but it is certain that the body loses more heat and has to supply this loss. Increase of appetite, improvement of digestion, circulation, sanguification, and metabolism are in vigorous persons generally the results of moderate degrees of cold. The opposite is often the case with delicate persons, and especially so when cold is combined with damp and wind. It is especially amongst old persons that the combination of cold with damp and high winds and absence of sun acts injuriously. The reports of the Registrar-General give ample proof of this. Thus in the last quarter of 1878, including two very cold months, the mortality of people above sixty was 24 per cent higher than in 1877, when the same period was characterised by mild weather. The rate of increase amongst people below sixty was only 8 per cent. However, by dryness of the air, light, sunshine, and absence of wind, moderate degrees of cold are rendered beneficial even to many delicate persons.

The fact that cold is disagreeable to many persons induces them to regard it as injurious. That this, however, is not the case, is proved by the fact that the mortality decreases as we proceed from the tropics towards the pole. We quote Michel Lévy's table in his *Hygiène*: —

From	0	to	20	degrees	latitude,	1	death in	25	inhabitants.
,,	20	,,	40	,,	,,	1	,,	,, 35·5	,,
,,	40	,,	60	,,	,,	1	,,	,, 43·2	,,
,,	60	,,	80	,,	,,	1	,,	,, 55	,,

[1] *Manual of Practical Hygiene*, 1878, p. 436.

It was formerly assumed that great equability of temperature is a necessary element of a climate useful in the treatment of chest complaints and *vice versa;* but this again is not correct. There may be great differences between sun heat and shade temperature, and still greater differences between day and night temperatures — as in Alpine climates in winter — and yet such climates exercise the most beneficial effects, provided the invalid can take sufficient shelter.

3. *The humidity of the air* is almost as important a factor of climate as the temperature. Watery vapour is always contained in the air, but its amount is constantly changing by the ceaseless processes of evaporation and condensation. The degree of absolute humidity varies with the seasons, and at different hours of the day; it is generally greater with higher temperatures and *vice versa.* The variations of relative humidity follow to some degree an opposite course: the relative humidity is, in general, lower in summer than in winter, and lower during the warmer parts of the day than during the colder; lowest, in fact, during the first hours of the afternoon and highest about sunrise. The variations are greater in summer than in winter, greater in inland than in marine climates; they are influenced by predominant winds.

Saturation of the air leads to *mists* and *clouds*, and the periods and frequency of their occurrence are of great importance in the appreciation of climates. Mists are more rare at considerable elevations above the sea; clouds are more frequent at certain medium elevations, changing with the seasons.

The rainfall varies considerably in different regions, from 0 in the desert of Sahara, and at some parts of the coast of Peru, to several hundred inches on the south-east slopes of the Himalayas, which are exposed to the moisture-laden monsoons. The amount of rain is not proportionate to the moisture of the air, for a region may be rainless, as Lima on the coast of Peru, in spite of a very humid atmosphere; and localities with considerable rainfall, like Genoa, may have tolerable dryness of soil and air. The number of rainy days does not correspond to the amount of rainfall. It may even be said, with some exceptions, that the number of rainy days increases with the distance from the equator, while the amount of rainfall decreases. The number of rainy days, the season when it rains oftenest, and the hours of the day on which the rain falls, are important matters to the invalid.

It is generally assumed that considerable rainfall is an injurious condition, but this is not always correct. Provided time enough be left for the invalid to take exercise and sit in the open air, rain is to some degree useful, as it has a purifying influence on the atmosphere. We must remember that Angus Smith found an increased amount of oxygen during and after rain, and cool and rainy summers in England mostly show smaller mortality than hot and dry ones. The notion that *snow* is injurious is even more incorrect. It is true that frequent melting of snow is apt to produce catarrh, but if the snow remain on the ground without melting for periods of several months, it is to many invalids a

source of benefit, for (*a*) it keeps the air free from the impurities rising from the soil, and from dust; (*b*) it increases the amount of radiant or sun heat by reflection; (*c*) it diminishes local currents of air by preventing the heating of the ground.

We have spoken of the moisture of the atmosphere as a great regulator of the distribution of warmth on the surface of the globe, and that it is as essential to man as to vegetation; but it is difficult to define accurately the effects on man of different degrees of moisture, because the factor of moisture cannot be separated from other factors, especially temperature, light, atmospheric pressure, wind. In dry air the evaporation from the skin and from the lungs is promoted, and this effect is increased if, at the same time, the sunshine be powerful, as in elevated regions. In moist air both are diminished. In moist and warm air the appetite and the vital energies become diminished, and there is often a tendency to diarrhœa and to affections of the abdominal organs. The development of low organisms is favoured in such climates, and this probably is the reason why in some such, as at Lima, tuberculosis is frequent and runs a most rapid course. In moist and cold air the evaporation from the skin is checked, the surface loses much warmth, and rheumatic and catarrhal complaints are common. Climates with a moderate amount of moisture are more equable by day and night, and in sun and shade; the evaporation also is slight; in dry climates, as we have already said, the opposite holds good. Climates with much moisture, especially with low temperatures, often have a very dull sky, which may shut out the light and heat of the sun for many days and weeks; such climates are not exhilarating, but with proper hygienic management may allow perfect maintenance of health and vigour.

4. Our knowledge of the effects of slight changes in the *atmospheric pressure* is not well defined; the effects of the great diminution of pressure at high elevations will be discussed under Alpine climates.

5. *Light* is of primary importance. As we all know, light is necessary for the development of chlorophyll in plants; and we meet persons frequently who after some dull days with absence of sun become depressed, disinclined to work, and dyspeptic, and who regain their energy with the return of the sun. We also often see home-sickness in natives of foreign and more sunny countries after some sunless weeks in London, which disappears after a few weeks of sunny weather; but though we may suppose that absence of sunshine is the principal cause of such mental and bodily disturbance, it is difficult to say how much is due to concomitant circumstances, such as excessive moisture and to low temperature. W. F. Edwards showed long ago that light is necessary for the development of the perfect form of the Batrachia. Moleschott, Pflüger, von Platen, Tubini, and others have found increased absorption of oxygen and excretion of carbonic acid under the influence of light in Batrachia and in some warm-blooded animals. H. Quincke's experiments prove that the oxidation of animal cells (of blood and pus) is increased under the influence of light. Many of the

effects of light on the animal organism are, no doubt, due to its action on the centripetal nerves, and especially on those of the retina; but the result of Quincke's researches, and also of those of other observers, show that light acts also directly on the cells and tissues without the influence of nerve centres.

The human body is influenced indirectly by the action of light on certain microbic parasites. Downes and Blunt, Arloing and Roux, had already shown that sunlight can kill bacteria, when Koch stated to the International Medical Congress at Berlin (1890) that it kills the tubercle bacillus within a very short time — varying from a few minutes to a few hours; and that even diffuse daylight does so, but requires from five to seven days. According to P. A. Komelevsky, solar light destroys the vitality of the Staphylococcus pyogenes aureus and albus, etc., in about six hours. He found that all portions of the spectrum powerfully affect the microbes, excepting the red and infra-red rays. Professor Marshall Ward showed by experiments that the blue rays of the spectrum have the greatest power in destroying bacteria; while the red, orange, yellow, and ultra-violet rays do not affect them; our present experience seems to him, however, not conclusive with regard to all varieties of microbes. Dr. Arthur Ransome communicated to the Royal Society in 1890 experiments on the action of soil, air, and light on the tubercle bacillus; and again Drs. Ransome and Delépine infer "(1) that finely-divided tuberculous matter — such as pure cultures of the bacillus, or 'tuberculous dust,' in daylight and in free currents of air — is rapidly deprived of virulence; (2) that even in the dark, although the action is retarded, fresh air has still some disinfecting influence; and (3) that in the absence of air, or in confined air, the bacillus retains its power for long periods of time." These experiences seem of great importance in the explanation of the aseptic nature of the air in the high Alps, on the Riviera, in the desert, etc. It may further be mentioned that Buchner has shown that direct as well as diffused sunlight very rapidly kills bacteria suspended in water.

There is yet a third kind of influence of light on the human body, namely, on the skin. John of Gaddesden, a court physician in the reigns of the Edwards ("Rosa Anglica"), in treating a royal prince, a son of Edward I., for small-pox, prevented scars by having the bed-curtains and all surroundings made of red colour. The same treatment has been pursued by N. Finsen[1] and Svensden,[2] with the result of preventing the suppurative stage and the pitting. This, if confirmed, may be explained by the exclusion of the chemical rays by the red curtains. On the irritating influence of these rays interesting experiments have been made by Drs. Bowles, Unna, Hammer, Finsen, and others. Dr. Bowles in his researches in the Alps on the effects of sunlight on the human body, was led to the conclusion that it is not heat, but those rays of shorter vibration at the violet end of the spectrum, which give rise to the phenomena

[1] *Hospitalstidende*, 1893.
[2] Den ledste Koppeepidemi i Bergen, *Medecinsk Revue*, October 1893.

of sunburn, and that rays reflected from snow are far more potent than rays direct from the sun, or those reflected from rocks. He found that various colours applied to the skin prevented the harmful rays from reaching the delicate nerves and vessels beneath the epidermis, and quotes a singular case of an Indian officer, who, having had repeated attacks of sunstroke, thinks that he has prevented the recurrence of the attacks by wearing an orange coloured lining to his clothes.

6. *Of Winds* — a large subject — we can only speak briefly. They are necessary as purifiers of the air, though they may under special circumstances carry malarial and other poisons. They often produce great and sudden changes in temperature, moisture, light, and atmospheric pressure; and bring with them, so to speak, the climates of distant regions. Before selecting a health resort the winds prevailing at different seasons, at different parts of the day, and their character, must be ascertained.

7. *Mountain chains* act as barriers to cold and to hot winds, and thus cause in the former case higher annual temperatures in the leeward localities, in the latter case lower. Their effects vary with their height, extension, abruptness, quality, and amount of vegetation; and with presence or absence of snow and glaciers. They exercise also a great influence on the quality of the atmosphere carried by the wind; they deprive, for instance, the moisture-laden, warm winds of a great part of their moisture, so that the climates to leeward of the chain are rendered drier and less equable.

8. Buchan (12 and 13) gives interesting facts on the effect of *drainage on the temperature of the soil.* The mean temperature of arable land is raised 0·80° F. by drainage; cold penetrates undrained more quickly than drained land; the temperature of drained land is more equable than that of undrained; in summer the temperature of drained land is occasionally raised 1·8° to 3° F. above that of undrained land. These facts may throw some light on the discoveries of Bowditch and Buchanan with regard to the diminution of phthisis mortality by drainage.

9. The presence or absence of *vegetation* exercises a marked influence in all climates. Bare surfaces differ according to the conducting power of the ground. The covering of the surface by vegetation prevents more or less completely the direct fall of the sun's rays on the ground itself, and thus prevents it from being heated to the same degree as bare rock or dry sand; and the plants themselves are never heated quite so much as bare ground on account of the constant process of evaporation. We have found the temperature above grass-land, and likewise clover, more than twenty degrees lower than above bare ground under great sun heat. The character of the vegetable covering, however, makes a considerable difference.

The influence of forests has been carefully studied by Buchan and Ebermayer (25). They found the temperature of the ground on which a forest stands to be several degrees lower than that of the neighbourhood. The difference is greater in summer than in winter, but the air within the forest has a lower annual mean. In summer the cooling

influence is specially marked during sunshine. The changes of temperature in forests are narrower and less sudden; the days are cooler, the nights warmer; the climate more equable. Trees acquire their maximum temperature in summer at about 9 P.M., while that of the air occurs between 2 and 3 P.M. "Hence trees may be regarded as reservoirs in which the heat of the day is closed up against the cold of the night." The relative humidity in forests is higher; in July about 10°, in January about 3·7°; forests lead also to increased rainfall; the air in forests being cooler and more saturated, the vapour of a moist wind on reaching a forest is condensed into mist and rain. There is less movement of air in forests, and they protect the adjacent land on the leeward side from winds and cold currents.

Second Section. — Principal Climatic Regions and Health Resorts

There are insurmountable difficulties in the classification of climates; the same degrees of latitude, for example, containing the most different climates. Many French writers, especially Lévy, Rochard, Fonssangrives and Lacassagne take the *mean annual temperature* with various modifications; but the mean annual temperature is an imperfect guide in the treatment of disease, for localities with the same annual mean often differ very widely in range at the same season or at different seasons. Thus Torquay, Paris, and Odessa have approximate annual means, but the following table shows how different are their seasonal ranges: —

Annual Temperature.	Winter.	Spring.	Summer.	Autumn.
Torquay about 52° Fahr.	44·0°	50·1°	61·3°	53·1°
Paris about 51·5° ,,	38·4°	50·4°	64·5°	52·0°
Odessa about 50·4° ,,	27·5°	45·8°	70·0°	50·7°

Thus the difference between summer and winter is for Torquay only 17°, for Paris 26°, for Odessa 42·5°.

A division according to the temperature of the seasons would be more useful, but places with the same winter temperatures may differ widely as to equability, sunshine, and humidity.

Several authors, English and foreign, adopt relative humidity as the main principle of classification (Vivenot, Walshe, Rohden, P. Niemeyer, Thomas), and this arrangement has its advantages; but other climatic factors may vary widely where the relative humidity is almost the same.

All such classifications appear to us so constrained that we should prefer to describe the several localities alphabetically; but this would lead to much repetition and require more space.

We therefore propose to follow, with some modifications, the plan

which has been adopted in previous treatises on this subject,[1] although we acknowledge its imperfections.

The sea exercises so powerful an influence on the climate of the localities adjacent to it that we will consider these under one great head — *Marine Climates* (in distinction from *Inland Climates*).

A. **Marine Climates.** — As fully marine climates can only be enjoyed on the ocean itself, we will begin with a short account of the ocean and such sea-voyages as are best adapted to invalids, and then consider the climates of small islands and the sea-coasts.

I. *The Ocean and Sea-Voyages.* — The climate of the ocean is characterised by warmth, equability, and considerable atmospheric moisture. Its physiological effects are sedative to the nervous system, while at the same time appetite and digestion are much improved. The aseptic character of the air, moreover, acts beneficially both upon the air passages and the system at large. The advantages which it offers are absolute repose and facilities for an open-air life. Its drawbacks are the confined sleeping space, the discomforts of cabin life in bad weather, and in some cases the monotonous character of the food.

The voyages most suitable to the invalid are practically four: — (1) the steamship voyage to the Cape of Good Hope; (2) the sailing voyage to Australia; (3) the steamship voyage to Australia; (4) the steamship voyage to New Zealand round the Cape.

The voyage to the Cape occupies about twenty days, and is thus too short for much benefit in serious cases; but it has great value as a remedy for overwork or tardy convalescence. The heat in the tropics is rarely injurious, and there is no sudden transition to cold.

The voyage to Australia on a sailing ship gives the full benefit of the marine climate. Two or three clipper ships, with special accommodation for invalids, sail in September or October. The outward voyage takes ninety to a hundred days. The log of one of these ships shows the highest temperature to have been 85° F., the lowest 49° F., while the difference between one day and another never amounted to more than 7° F. (109). Except in a long calm in the equatorial belt the heat is not severely felt. To obtain the benefit of the change the patient should be moderate in his diet and take sufficient daily exercise. With such precautions selected cases will derive the greatest benefit from the life. The drawbacks to the voyage are the monotony of the life and the lack of fresh food. The return voyage might be made in a sailing ship round the Cape, or by steamer. A return by Cape Horn is always unsuitable. The steamship voyage offers more frequent places of call, and more frequent supply of fresh meat and vegetables. On the other hand greater heat is experienced (in the Red Sea), and the greater speed of the vessel makes the changes of climate more sudden. The transition from the Suez Canal to the Mediterranean is a considerable danger on the

[1] "Klimato-Therapie" in Ziemssen's *Handbuch der allgemeinen Therapie*, vol. ii. part 1, 1880, English translation by Dr. Port: Smith, Elder and Co., 1885. And in "Climate and Health Resorts" in the *Book of Health*. Cassel and Co., London, 1883.

return journey. In modern ships the smoke from the engines is no longer a real drawback. The times of departure and return must be carefully chosen in order to avoid the hot months in the Red Sea and the monsoon in the Indian Ocean; it is wiser to return by San Francisco than to pass through the Red Sea in the hot months.

In the steamship voyage to New Zealand the weather encountered is very similar to that met with in the sailing voyage, but is shorter, and the food more varied.

We may add that in exceptional cases of hardy invalids summer voyages with whalers to the northern seas have been tried with fairly good results.

In the summer months yachting around the coasts of England, Sweden, Norway, and the north of France offers a good chance for enjoying the advantages of marine climates without much risk.

A combination of yachting with residence on land may occasionally be carried out with great advantage in the Mediterranean during the colder months.

II. *Coast Climates, including small Islands.* — These climates, greatly though they differ amongst themselves, have some points in common: (1) The air is comparatively free from organic dust; (2) it contains a larger amount of moisture owing to the constant evaporation from the surface of the sea, and the amount of moisture does not vary much; (3) there is a constant renewal of the atmosphere by the air currents; (4) there is greater equability of temperature, not only between different seasons, but also between the different parts of day and night, when compared with inland climates.

A striking instance of this equability of a climate almost entirely marine is given by A. Buchan (in his suggestive article on "Climate" in the *Encyclopædia Britannica*) in the island of Monach, situated about seven miles westward from the Hebrides, between 57° and 58° N. "in the full sweep of the westerly winds of the Atlantic which there prevail. The mean January temperature is 43·4°, being 1·8° higher than the mean of January at Ventnor, Isle of Wight (nearly seven degrees farther south), 0·8° higher than that of Jersey and Guernsey." On the other hand, the mean temperature of July is 55·0° at Monach and 62·4° at Ventnor. Monach has therefore warmer winters and cooler summers than an ordinary coast climate farther south.

The effects of the sea-side, although varying considerably according to constitutions and localities, may be said to improve the appetite, the mental and bodily energy, the condition of the skin, the sleep, and metabolism of tissues. Such changes are very useful in many cases of weakness without actual disease, during convalescence from disease, in climacteric conditions, and in people who are said to be "run down" from work or social exertions and worry. These climates are invaluable in the physical training of children disposed to scrofulous diseases and allied conditions. They require, however, a certain degree of resistance, and, in many persons, special attention to the action of the bowels. They are

mostly unsuitable for chronic affections of the heart with great dilatation, for some kinds of asthma, and for skin diseases. Although the numerous varieties in the climatic conditions of different marine regions render subdivision necessary, yet different localities in the same region and very near to one another may present varieties of climatic elements, such as aspect, elevation, degree of shelter, and so forth.

As the degree of humidity of the air exercises great influence on the equability of climates and on the functions of the body, we will adopt it with C. T. Williams, Thomas, and others, as the principle of the greater subdivisions, and use the differences of temperature for the formation of sub-classes.

If we adopt as subdivisions: 1. Humid marine climates; 2. Marine climates with moderate or slight humidity, we must confess that no thorough lines of demarcation can be drawn, and that some of the localities placed in sub. 1 might claim a place in sub. 2.

1. Humid Marine Climates. — There are great differences in this subdivision according to the temperature. We are, however, principally concerned with the *warmer* climates, of which *Madeira* may be taken as a type. The opinions on the climato-therapeutic value of Madeira have varied considerably. In former years it was considered by many authors as the best climate for consumption, while at present many regard it as the worst. We will endeavour to give a short description, and refer for further information to the works of Renton, Clark, Mittermaier, Lund, Grabham, Goldschmidt, Langerhans, and others. The Madeira Islands are situated between 32° and 34° N. and between 16° and 17° W. The climate of Funchal, the principal town, is remarkably equable; the mean moisture varies between 70° and 74°, but is subject to variations from air currents. The number of rainy days is mostly above fifty. The mean annual temperature is 65° F. — winter about 61°, spring 62°, summer 69·5°, autumn 67°. Lowest night temperature rarely below 43°; highest day rarely above 86°. Mean differences between night and day about 9°, from one day to another about 1·1°. Funchal is not exempt from winds, but the air is usually calm from 7 to 9 A.M., at which hour sea-breezes blow till 3 P.M.; land winds set in later at night. The air is free from dust and rich in ozone; the character of the climate is sedative, to some people relaxing. It has great power to allay coughs in chronic catarrh with irritability of the mucous membrane; but many people after some weeks feel depressed, lose appetite, and have a tendency to diarrhœa. A disadvantage of Funchal is the steepness of the hillside on which it lies, and the consequent difficulty of getting above the houses on foot.

As to the effect on tubercular consumption, the result of the experiment made by the authorities of the Brompton Hospital on twenty selected cases of consumption has not been satisfactory, and we know ourselves of a rather large proportion of unfavourable cases; but, on the other hand, we have seen better effects than at most other places in elderly persons with much loss of lung and emphysema, in complica-

tions with albuminuria, and in weak and irritable people with rapid pulse (the erethic type). The beauty of the vegetation, the scenery, and the easy life of Madeira exercise on some persons so great a charm that it is impossible to dissuade them from going thither, even if they are told that they could do better elsewhere. More than once, especially in former years, patients would tell us they would rather die in the enjoyment of the sub-tropical beauty of Funchal than fight for life in the "ice-bound Alps," or at the "dusty Riviera," or in "sunless England." And such mental conditions have a claim on our sympathy. This climate is more generally beneficial in cases of chronic bronchial and laryngeal catarrh, and in emphysema with scanty expectoration than in pulmonary tuberculosis; but in cases with copious discharges from the mucous membranes, atonic dyspepsia, and tendency to diarrhœa, Madeira and allied climates are to be avoided.

Similar remarks may be applied to the *Azores*, which are little used as climatic resorts.

The *Canaries*, with *Teneriffe* and the *Grand Canary*, have in common with Madeira the equability of the climate, but have a slightly higher temperature and are decidedly drier, so that they might claim a place in the subdivision of moderate humidity. They are mentioned here principally on account of their situation near Madeira. The heat of the day is tempered and the coolness of the night is diminished on Teneriffe by a layer of mist between 3000 and 5000 feet above the sea-level. On the Peak, above this layer of mist, Dr. Marcet found the climatic conditions very different, viz., hot days, cold nights, and great dryness of air. The Canaries have a greater claim as health resorts than Madeira, and offer good accommodation, but are much wanting in means of amusement (53, 35, 60).

Of *Mogador*, on the north-west coast of Africa, we owe a written account, based on personal experience, to the late Dr. Leared, who describes it as one of the most equable climates. Mean annual temperature 67° F., mean winter 61°, mean summer 72°, mean hottest month 80°, mean coolest 59°, relative humidity 78°. Number of rainy days 44, of clear days 270. It is under the influence of the Atlantic; is sheltered from the desert winds by the Atlas chain. Accommodation is as yet limited.

Cadiz, on the island of Leon, on the south-west coast of Spain, may be placed in this group. It partakes of the character of the Atlantic as well as of the Mediterranean, has about one hundred rainy days in the year, and an average relative humidity of 76°; the mean winter and spring temperatures are about 59° F.; the average daily range is only 10·5° F. We have seen some satisfactory results from this resort in early cases of consumption in weakly and irritable persons, but the hotels are situated in the midst of the town, and are scarcely suitable to invalids. Only persons, therefore, who have to earn their livelihood at the place ought to be sent there. *San Lucar*, in the same region, with a similar but somewhat drier climate, is recommended by Spanish physicians at the commencement of tubercular phthisis.

In the *southern hemisphere*, where the sea predominates more than in the northern, there are several islands with moist and warm climates, which under especial circumstances may be used as health resorts, especially *Tahiti*, in the Society Islands, the *Tristan d'Acunha* group, the *Feejee* (Fidji, Fiji, or Viti), the *Friendly* or *Tonga Islands;* but the accommodation and hygienic conditions are as yet defective.

The groups of islands situated to the east of Central America, and comprised under the collective name of the *West Indies* (from 10° to 27° N.L.) find a place among the warm and humid marine climates. They possess rather uniform high temperatures, varying in the different islands between about 68° F. and 83° F. Their action is rather sedative and relaxing. Diseases of the digestive organs are prevalent; and only in exceptional cases can they be recommended to invalids suffering from irritable catarrhs of the respiratory mucous membranes. Dr. C. T. Williams (105) reports a favourable result in a consumptive young physician at Jamaica; R. H. Bakewell (*Practitioner*, 1878) has a rather high opinion of Barbados; and we have ourselves seen some fairly satisfactory results in emphysema with chronic pulmonary catarrh, and in two cases of phthisis — one at Jamaica, the other at Barbados; but unfavourable results have prevailed in our experience, especially through failure of the digestive system with loss of appetite and chronic diarrhœa, so that we can scarcely recommend these localities excepting in cases where the choice of climate is limited by other circumstances.

The climate of the peninsula of *Florida*, extending from 24° to 31° N., resembles that of the West Indies, but is less relaxing. In July, August, and September fevers are prevalent, but they are rare during the remainder of the year. Florida enjoys some reputation in North America as a mild winter resort for delicate persons suffering from emphysema, chronic bronchial catarrh, and early phthisis. The adjacent coasts of *Georgia* and *South Carolina* have somewhat similar climates, but they are more under the influence of the continent, and have lower average temperature and humidity.

Humid and cool marine climates are rarely used in climatic treatment, but they are very interesting on account of their great equability of temperature. The best known localities belonging to Europe are the Hebrides, the Orkneys, the Shetland Islands, the Faroe Islands and Iceland; and in the southern hemisphere the Auckland and Falkland Islands.

2. Marine Climates with Moderate or Slight Humidity. — Amongst the warmer localities of this sub-section those of the *Mediterranean coasts* are of the greatest interest to us. They are all under the powerful influence of this remarkable inland sea, which differs from the Atlantic and Pacific in its freedom from polar currents, and in its temperature which down to its greatest depths (1500 to 2000 fathoms) is 54° to 56°; while in the Atlantic, outside the Straits of Gibraltar, the temperature at the same depth is only 35·6° to 37°. The Strait of Gibraltar is so shallow that it does not admit the polar stream of the Atlantic.

Although all the localities on the shores of the Mediterranean have

some points in common, yet the several tracts offer considerable differences. The Riviera has the first claim on our attention.

The *Riviera* stretches from Toulon to Genoa. The region consists for the most part of a plain from two to four miles in width, extending from the sea to the lower spurs of the mountains which everywhere guard the coast. From these lower slopes the mountains rise rather steeply to a height of from 2000 to 3000 feet, affording everywhere a shelter from the north, and generally from the north-east and north-west. The coast consists of a series of headlands, between which stretch gently-curved bays, on whose shores the main resorts are situated. The characteristics of the climate are as follows: —

(*a*) *Warmth.* — Greater than that of other localities in the same latitude. This greater warmth is due to three causes: (1) The complete shelter from northerly winds; (2) Radiation from the mountains during the colder parts of the day and year; (3) The presence of the Mediterranean Sea, which is some 5° warmer than the atmosphere. The mean temperature for the six winter months varies from 50·8° to 51·5°; for the months of December, January, and February, it varies from 47° to 49° F.

(*b*) *Dryness.* — Unlike most of the marine climates, the Riviera is distinguished for its dryness, the mean relative humidity being about 65° to 70° during the winter months.

(*c*) *Abundant Sunshine.* — During the six months of winter generally from 100 to 120 days are fine.

(*d*) *Small Rainfall.* — With few rainy days, the rainfall varies from 28 to 31 inches, and a great part of this falls between the end of September and the beginning of November. In such a climate some hours of almost every day can be passed out of doors.

There are, however, several very distinct drawbacks to the climate: (*α*) The great frequency of high winds, principally in the spring, mainly from the north-east and north-west. (*β*) The great difference between sun and shade temperature, thus increasing the danger of chill. (*γ*) The rapid fall of temperature at sunset, which compels the invalid to return home before that hour.

The physiological effects of the climate are exerted for the most part on the nervous system; the climate is, with a good deal of truth, described as exciting. Sleeplessness is a common complaint on first reaching the coast, but in most cases soon passes off. Neuralgia, on the other hand, is often aggravated, and any hysterical or melancholic tendency is frequently made worse. Most persons, however, feel invigorated both in mind and body. Considerable care is necessary to avoid catching a chill. Exposure to sudden changes of temperature does not so frequently lead to a cold in the head, or tracheo-bronchitis, as at home, but more often causes an attack of diarrhœa or even of colitis.

The several resorts to be considered are: —

(i.) *Hyères*, situated about three miles from the sea. The mean winter temperature is 50·6° F. (Biden). Relative humidity 73°. It is not, however, very well protected from the north, and is much exposed to the

north-west, whence the mistral blows in the spring. In other respects, being somewhat more distant from the sea, it is not so exciting as are the other resorts; patients sleep better, and hysterical women suffer no aggravation of their symptoms.

(ii.) *Costa Belle*, nearer the sea, is much better protected from winds, is more wooded, and not quite so dry.

(iii.) *St. Raphael* and *Valescure*, near Frejus. The former is near the sea-shore, the latter some short distance inland. They are not very well protected by mountains, but are surrounded by pine woods. The mean temperature is somewhat lower than that of the other resorts. They are better suited, perhaps, to a more vigorous class of case, and are not so exciting as the more easterly resorts. Some forms of asthma, neuralgia, and irritability of the skin do better there than at the more eastern places of the Riviera di Ponente.

(iv.) *Cannes* has a mean temperature of 50·85° for six winter months, and a mean relative humidity of 73° (53); it is the largest of the mere health resort towns along the coast. To the north the protection is not by any means complete; the higher ridges of the Alps are too far removed from the sea to afford adequate shelter from this quarter. It is well protected, however, on the east and west. The mistral blows frequently in February and March. The majority of the patients find the climate bracing to the body and exhilarating to the mind, but it possesses to a marked degree the quality of an excitant to the nervous system. Invalids requiring much shelter can do better elsewhere than at Cannes; on the other hand, patients who require a bracing and yet warm climate will fare better at Cannes. Cannes enjoys the advantage of offering several residential localities with distinct varieties of climate. There is a warmer district near the sea, while more bracing and less exciting situations inland can be found on the Californie and in the district of Cannet. Patients who find the sea-shore too exciting often benefit by a removal to the latter.

(v.) *Grasse*, situated behind Cannes at an elevation of 1000 feet, possesses a cooler climate, and forms a useful intermediate station during April and May for patients who find the heat in those months already too oppressive at Cannes.

(vi.) *Antibes*, situated on the headland of that name, now possesses an excellent hotel. It is perhaps not sufficiently sheltered for serious invalids, but hardier ones find it a pleasant climate and the centre of beautiful excursions.

(vii.) *Nice*, the largest town upon the coast, was formerly also its principal health resort. Latterly, however, it has somewhat fallen into disfavour on account of the piercing winds which visit it in winter and the irritating dust of the roads. The suburbs, however, of Carabacel, Cimiez, and Mont Boron present many attractions; they are moderately sheltered and possess one advantage, namely, distance from the sea. Some persons when residing near the sea always suffer from constipation or other digestive disturbance, or are troubled by insomnia. Such

symptoms are often entirely removed by a change to a residence a mile or two inland.

(viii.) *Villefranche* and *Beaulieu* lie between Nice and Monaco; both possess considerable advantages as to shelter and temperature.

(ix.) *Monte Carlo* is certainly one of the most sheltered situations on the coast. The presence of the gaming tables, however, offers an insuperable objection to its being seriously considered as a health resort.

(x.) *Mentone.* — Mean temperature for winter months 51·5°, mean relative humidity 72·8°.[1] This place, owing to the advocacy of the late Henry Bennet, has perhaps obtained the greatest celebrity as a health resort. The town proper is situated on a tongue of land, which separates the bay into an eastern and western portion. The eastern bay of Mentone is admirably sheltered, the mountains rising on all sides sharply from the sea. It possesses the warmest temperature for the winter months of any resort on the Riviera. For cases requiring absolute shelter and warmth it is superior to any locality on the coast. Many persons, however, find it relaxing, while the steep rise of the mountains compels a residence close to the sea, with the ill effects which such a position exerts upon some temperaments. On the whole, however, in those qualities by virtue of which the Riviera climate is most to be esteemed it may be considered rich. The western bay, on the other hand, is less sheltered and more bracing, and, owing to the larger space away from the sea, is adapted to a larger number of cases, though not so peculiarly suitable for a few. *Cap Martin*, in the vicinity, must also be mentioned.

(xi.) *Bordighera* is well protected from the north-east and the west, but through the valleys in the north-west the wind finds access. The chief hotels and villas, however, are not situated by the sea-shore, and by the intervention of a spur of the mountains obtain adequate protection from that quarter. The temperature is for the winter months somewhat lower than at Mentone, but the climate is more bracing. The exciting effects of the Riviera climate are also not so marked as at places farther westward.

(xii.) *San Remo* has a mean temperature for six months of 50·55° (36); a mean relative humidity of 68°. It lies eight miles from Bordighera, and well sheltered from the north and north-west, the mistral occurring but once or twice in the winter months. On the other hand the east wind is prevalent. The exciting effects of the climate are not so marked, but to some cases it will not be found so well adapted as the east bay of Mentone.

(xiii.) *Alassio*, twenty-eight miles east of San Remo, is well sheltered from the north and north-west and west; it is, however, exposed to the east and north-east. The lower spurs of the mountains are admirably sheltered from this quarter, but unfortunately all the hotels are situated on the sea-shore, and are consequently exposed.

(xiv.) *Pegli*, six miles from Genoa, the last of the resorts on the

[1] Andrew, quoted by Marcet.

Western Riviera, is sheltered on the north, north-west, and west, but exposed to the east. It is, however, not sufficiently organised for the reception of other than the hardier class of invalids. The climate is more humid and less exciting than the westerly resorts.

By the end of October the weather will be cool enough to render any of these resorts suitable for invalids. It is rarely prudent to prolong the stay beyond the end of April, and never to spend the summer on the coast.

Eastern Riviera. — The continuation of the coast-line from Genoa to Pisa, usually called the *Riviera di Levante*, is less dry than that between Cannes and San Remo, and somewhat less protected from cold winds, the mountain chain being low and broken; otherwise there is some similarity between them. *Nervi*, near Genoa, has the principal claim as a health resort. It is fairly well protected from cold winds, and is less exciting than the majority of localities on the Western Riviera. The mountains come so near to the coast that the excursions for the invalid are limited; but those requiring repose find it helpful, the more so as there is not much temptation to social dissipation. Other localities picturesquely situated, but not so well protected, are *Spezia*, *Chiavari*, *Rapallo*, and *Santa Margherita*. A rising health resort, for bathing in summer and shelter in winter, is *Viareggio*, about twelve miles north of Pisa. The shelter is principally due to the large pine forests in the neighbourhood.

Pisa, although six miles from the sea, may likewise be mentioned here, since the climate partakes both of marine and of inland characters. It is rather humid, and not well protected; the sky is often dull, but it is comparatively free from mists. The winter temperature is about 2° to 2½° lower than at the Western Riviera. It is now less frequented than in former years.

Genoa and Leghorn are too much exposed to be regarded as health resorts.

Southern Italy is rich in charms of nature and historical associations. The accommodation at the principal places is good, and the hygienic arrangements are improving; the climate is sunny, but by no means free from cold northerly and north-westerly winds, especially in spring. *Naples* has considerably gained of late by a good water supply. *Castellamare*, *Sorrento*, and *Amalfi* have good autumn climates, and Amalfi is also well sheltered in spring. The islands of *Capri* and *Ischia* have many attractions, but are not sufficiently sheltered from cold winds, nor are they, as yet, thoroughly hygienic.

The *island of Sicily* is not much recommended by English physicians, nor can careful medical supervision be had there; but the great beauty of the country, and the many historical and archæological points of interest, have their favourable influence, and, combined with light and sun, have led to recovery or great improvement in many cases of overwork, of invalidism allied to the neurasthenic type, of rheumatism, slighter degrees of glycosuria, and tendency to premature senile decay in its

various forms. The sirocco is occasionally irritating and depressing. Rain rarely falls in summer, but abundantly in late autumn and winter. The mean humidity is moderate — rather higher at *Palermo* and the north coast than on the east coast. Good accommodation, with fair sanitary arrangements, is to be found at *Palermo, Taormina, Acireale, Catania,* and *Syracuse.* The Hôtel des Temples at Girgenti is now open again.

On the south-west of the Mediterranean, *Tangiers* in Morocco is under the combined influence of the Atlantic and the Mediterranean, and, owing to the former, approaches more the humid than the dry class of marine climates. The winter temperature lies between 57° and 62°; the principal rains in November and December. The late Dr. Leared and most of those who have resided there describe the winter and spring as delightful. The absence of carriage roads and the want of public security are for the present great drawbacks to its usefulness.

Gibraltar may be mentioned in this group, but it can scarcely be called a health resort.

Valencia has often been recommended on account of its mild and equable climate, but the effects of the irrigation of adjacent rice fields are injurious to most invalids. *Barcelona* is rathered sheltered by a range of hills from northerly winds, has good accommodation and fine walks. *Alicante,* like the whole coast of Murcia, is rather more dry. *Malaga* is described by Dr. Francis, who has studied the climates of Spain, as the mildest place in Europe; it has a dry soil, a south-eastern aspect, and is surrounded by a semicircle of mountains, but it is not sufficiently sheltered from the cold north-west winds. The temperature in winter is about 55° F., in spring 62°; the daily range scarcely 5°. The number of rainy days is about 40.

Algiers consists of the old Moorish town and the French settlement, of which the slope of *Mustapha Supérieur* and the road thence to *El Biar* are the most satisfactory localities for residence. The mean temperature during the invalid season, from the end of October to the end of April, is about 57° to 52° F., and the average number of rainy days is between 45 and 65. The soil is so porous that the rain seldom keeps an invalid at home the whole day. Rain usually falls heavily; there is rarely a drizzle. The sirocco is rare during the invalid season, but it blows occasionally, and exerts on some persons a relaxing effect, being hot, sultry, and dry. At few places is the difference of winters so great as at Algiers; two seasons are rarely alike. As a rule, however, November, April, and part of May are like a fine summer in England; December to March like autumn, but with a greater share of sunshine. The air of Algiers is much less dry than at the Western Riviera; the hills are covered with evergreen shrubs and woods. The neighbourhood of Mustapha is rich in beautiful walks, and good carriage roads extend in every direction.

People who stay the winter in Algiers may spend part of their time at *Hammam Meskouttin* or *Hamman R'Irha,* with their well-known hot springs; or at Biskra.

Biskra, a place of growing importance, is a union of several villages or urban quarters, lying among plantations of date-palms and evergreen trees, N. lat. 34° 51′, on the outskirts of the Algerian Sahara, at an elevation of about 360 feet above sea-level. It thus partakes of the characters of desert climates, excepting when northern winds prevail; and enjoys during the six colder months of the year many climatic advantages. It is much drier and sunnier than the neighbourhood of Algiers itself; but it is subject to violent winds which for days together may prevent outdoor exercise. Another disadvantage is that the water contains too much salt for drinking and some cooking purposes. There is good hotel accommodation, and the place is likely to become a satisfactory health resort for fairly hardy invalids requiring warm and dry air. The railway journey occupies at present from Algiers two days, from Constantine one. There are hot springs a few miles from Biskra, at "Fontaine chaude," *Hammam Salahin* ("Bath of the Saints") but the arrangements are not yet suited even for moderately fastidious people.

The Slopes of the Lebanon offer an excellent climate, only varying with the height above sea-level — the higher, of course, the colder. The view of the hills and of the sea below is glorious. In the summer months grapes, figs, and other fruits abound. The hotels are said to be good, especially at Alai, three hours' drive above Beyrout (or two hours by the new railway). The cost of board and lodging is usually about seven shillings a day per head. Dr. Canney, of Luxor, tells us that Brumana, on a fir-clad crest near Beyrout, is a pleasant health resort, and probably a little better than Alai.

Ajaccio in Corsica has a mean annual temperature of 62·5° F. — autumn 66·7°, winter 52°, spring 60·3°, summer 76·7°. The number of clear sunny days is great; the humidity is greater than on the Riviera. It is almost completely protected from cold winds. The accommodation is good. The climate is less exciting than that of the Riviera, and some invalids, who suffer from sleeplessness and neuralgia at the Riviera, feel better at Ajaccio. The best time is from the beginning of November to the middle of April. Summer stations can be found on the mountains for those who are not fastidious.

The *Sanguinaires*, small rocky islands near Ajaccio, have a still more decided marine climate, but the accommodation is as yet poor.

The climates of the shores and islands of the *Adriatic* Sea are very different from those on the western side of Italy. The predominant defects are the prevalence of the dry and cold wind from the north, the bora or tramontana — a land wind; and the moist and warm sirocco — a sea-wind. The change between these two winds is accompanied by great variations in the temperature and in the relative humidity of the air, which are not well borne in irritable states of the nervous system or by pulmonary invalids.

Venice, the best known of these localities, enjoyed in former years a great reputation in the treatment of consumption, and has the advantage

of being free from dust and having good accommodation and artistic attractions. *Goerz*, near the north-west corner of the Adriatic, and *Volosca* and *Abbazia* near the north-east shore, possess some shelter and beautiful positions, but cannot compete for English invalids with the Riviera di Ponente. Amongst the islands only *Lesina* and *Lissa* need be mentioned; they possess rather more equable climates than the shores, and some accommodation.

In the *Ionian Islands* the only place which has some pretension to be a health resort is *Corfu*. The beauty of the position of the town of Corfu is great, and the whole island is beautiful; but it is too much exposed to wind, and the temperature and humidity of air vary considerably.

The *south-west coast of France* possesses a few localities which deserve to be mentioned.

Biarritz is fully exposed to the influence of the Atlantic; it is bright, and exercises on most people a bracing influence in spite of a rather high degree of humidity and frequent rains. It is not suitable to persons requiring shelter; but many old Indians with their complicated cachexias derive much benefit from this climate, which also offers a useful change to invalids wintering at Pau and Arcachon. *St. Jean de Luz*, a little to the south of Biarritz, has a similar climate.

A different kind of climate is that of *Arcachon*, which is situated on the shores of a large basin of salt water connected with the actual sea by a narrow channel. The influence of the sea is, therefore, considerably modified. The houses of Arcachon lie within a large pine forest, which is spread over the extensive dunes of the Atlantic. It is thus protected from the violence of the Atlantic winds, and the inland winds, too, are greatly mitigated by the trees. The climate is rather humid, equable, and unirritating, and the air in the "ville d'hiver" is impregnated with emanations from the pine-trees.

The western portion of *Southern California* presents several localities suitable for invalid residence. The country consists of a wide, fertile plain intersected by the lower spurs of the Sierra Madre and the coast range. The climate is warm and dry, with a large proportion of sunshine and small rainfall. The daily range is considerable, the prevalent westerly wind causing a fall of temperature in the afternoon. The damp, chilling sea-fogs, rolling in from the Pacific, are a drawback. On the other hand, the variety of elevation within a comparatively small compass fits it admirably for an all the year round residence. According to Dr. Davidson (16) a few hours' ride enables one to escape from the heat of summer to a cool and bracing atmosphere. Presenting some resemblance in climate to the Riviera, it shares some of its drawbacks, treachery amongst them. Very good results, however, are reported in cases of phthisis, while its fruit-growing industries offer a means of livelihood and permanent occupation. Dr. Davidson cautions the invalid against staying near the coast; the best residences are sheltered spots in the foot-hills or at the base of the mountains.

The chief resorts where good accommodation can be had are: —

Los Angeles, with a mean annual temperature of 61° and relative humidity of 69°; its suburb, *Pasadena*, at an elevation of 830 feet, may also be mentioned. *San Diego* has a temperature of 54° in January and 69° in August; *Santa Barbara*, on the coast plain, a temperature of 50° to 55° in winter and 65° to 70° in summer.

The coast climates of Great Britain and Ireland may be placed among the cooler marine climates with moderate humidity. Some localities might more justly find a place amongst the humid climates, but for the sake of brevity we will consider them together. Between the coasts of these islands there are considerable differences, especially between the resorts on the east coast and those on the west; but certain features more or less common to all give them a special character. The mean temperature is much higher than is due to latitude. This is strikingly illustrated by A. Buchan. "If no more heat were received than is due to the position on the globe in respect to latitude, the mean winter temperature of Shetland would be only 3°, and that of London 17°. But chiefly owing to the heat given out by the Gulf Stream during winter, and carried to the places by the winds, their winter temperatures are respectively 39° and 38° — Shetland being benefited 36° and London 21° from their proximity to the warm waters of the Atlantic." Part of this increase of temperature is due to the actual contact with the warmer sea.

Mild winters and cool summers, comparative absence of extremes, and a rather humid air, with many rainy days and comparatively many rainy hours, are the effects of these influences. The air, rich in water vapour, is less transcalent and translucent than in drier regions; hence direct sunheat and sunlight are less than on the Alps (Waters and Frankland) and on the Riviera (Marcet). On the other hand, the water vapour checks radiation at night and equalises the temperature of night and day. The chill at sunset is less than on the brighter and drier Riviera. The climatic characteristics are, therefore, comparatively high annual temperature, a fairly high degree of humidity, great equability as regards seasons and periods of the day, dulness of atmosphere with but a small amount of direct sunlight and sunheat, and more than average windiness. The combined effect produces health-giving and tonic, though not uniformly agreeable and exhilarating climates, which require some vigour of constitution to bear them. Speaking roughly, we may designate the west coast as warm and moist, the east as dry and cold; the western part of the south coast, as far as Sidmouth, as moist and specially warm; the line from Bournemouth to Hastings, including the Isle of Wight, as fairly dry and warm; the south-eastern part, with Folkestone and Dover, as approaching the characters of the east coast.

During the early part of the winter the temperature on the west and south-west coasts of England is between 2° and 6° higher than on the east coasts; it gradually rises from the south-east to the south-west coasts. Towards summer this difference gradually disappears, and then sometimes the east coasts are warmer than the west.

We may roughly divide the sea-side resorts into (*a*) *summer* and (*b*) *winter resorts* — adding, however, that some of the latter can occasionally be beneficially employed in summer, and *vice versa*.

(*a*) *Summer Resorts.* — There is no other country which is so well provided with good summer sea-side places. The majority of them are situated on the east coast, and are decidedly bracing. Going from north to south we have Nairn, St. Andrews, Portobello, North Berwick, Redcar, Saltburn, Whitby, Scarborough, Filey, Bridlington, Hunstanton, Cromer, Yarmouth, Lowestoft, Aldborough, Felixstowe, Walton, Westgate, Margate, Broadstairs, Ramsgate, St. Lawrence, Deal, Walmer and St. Margaret's. On the south-east and south coasts, Dover, Folkestone, Sandgate, Hythe, Eastbourne, Seaford, Brighton, Worthing and Littlehampton, Bognor, Southsea. In the Isle of Wight, Sea View, Cowes, Ryde, Alum Bay, Freshwater, Sandown and Shanklin; farther west, Swanage, Weymouth, Lyme Regis, Seaton, Exmouth; the Channel Islands; New Quay and Bude, Ilfracombe and Lynton on the north coasts of Cornwall and Devon; Minehead, Weston-super-Mare, Clevedon and Portishead on the Bristol Channel; Tenby, Aberystwith, Barmouth, Beaumaris, Penmaenmawr, Llandudno, in Wales; Southport and Grange-over-Sands in Lancashire; Douglas and Ramsay on the Isle of Man have almost thoroughly marine climates. Silloth in Cumberland, and Ardrossan, Oban, and Rothesay on Bute in Scotland have cool and rather humid summers, the last has mild autumns and winters.

The coasts of Ireland possess a mild, equable and rather humid climate; Bray, Howth, Kingstown, Dundrum, Holywood, Queenstown and Glengariff are good representatives; Bundoran and Kilkee are under the full influence of the Atlantic; Port Rush and Port Stewart in the north are somewhat more bracing; Rostrevor and Warrenpoint are not quite exposed to the sea, and offer the advantages of beautiful inland country, protection from wind, and modified influence of the sea-air.

(*b*) *Winter Resorts.* — If we proceed from east to west we begin with Hastings and St. Leonard's, which are less warm and somewhat more bracing than the localities farther west and south-west, and would be similar to the other places on the south-east coast were it not for the greater shelter which the Downs afford from north-west, north, and north-east winds. Those requiring a warm, humid and equable atmosphere are better farther west and south-west, but cases of atonic catarrh of the mucous membranes are mostly benefited in the autumn and winter, up to the end of February when the east winds begin.

The Undercliff on the Isle of Wight, and the fair results obtained at the National Hospital for Consumption at Ventnor, are well known. This is also the case with Bournemouth and Boscombe, which offer abundant accommodation at the hotels and in numerous villas scattered about on the cliffs and in the pine woods; these unfortunately are suffering from the rapid increase of the buildings.

Salcombe, Sidmouth, Budleigh-Salterton, Exmouth, Dawlish and Teignmouth have all fairly warm and equable winters; and in their

climatic characters resemble Torquay, which, however, by its situation in a large bay surrounded by three hills, offers opportunities for extensive exercise on level as well as on rising ground, with ever varying beautiful views. In spring the east wind sweeps round the protecting rocks and promontories, but is felt less severely than on the eastern part of the coast. Farther west Falmouth in Cornwall claims our attention by similar qualities, and Penzance, which has less shelter from wind, but fair equability of temperature. On the coast of Wales, Pwllheli on the Cardigan Bay deserves our appreciation by its sheltered situation from north and east winds; and Llandudno, although principally a summer resort, offers also some advantages in winter. Grange on Morecambe Bay has good shelter. More northward the coast and the islands on the west of Scotland have a remarkably mild and equable, but at the same time humid winter climate; Rothesay, on the island of Bute, offers the best accommodation. Glengariff and Queenstown in Ireland, among the humid climates, have good claims to be regarded as winter resorts.

The climate of the north and still more of the north-west coast of France has, owing to the Gulf Stream, some analogy to that of the south and south-west coast of England, especially in summer. There is very little shelter in winter, but the climate in summer is rather more dry and stimulating than on the opposite coast of England. Dinard, Cabourg, Houlgate, Villers-sur-Mer, Trouville, Deauville, Étretat, Fécamp, Dieppe, St. Valéry en Caux, Tréport and Boulogne offer satisfactory accommodation and good sands for bathing. The same may be said of Ostend, Blankenberghe and Heyst in Belgium, and Scheveningen on the Dutch coast.

More bracing still are the sea-side and island resorts on the north coast of Germany, exposed to the German Ocean; Borkum, Norderney, Baltrum, Langeroog, Spikeroog, Wangeroog, Wyk on Föhr and Westerland on Sylt, but the accommodation at them is often primitive. The island of Heligoland has a much more decided marine climate.

The shores of the Baltic are less stimulating, but have beautiful forests.

B. **Inland Climates.** — We must be satisfied with the subdivision of the great variety of these climates into, I. Elevated or Mountain climates, and II. Lowland or Plain climates.

I. Elevated or Mountain Climates. — Great as is the difference between the various resorts belonging to this subdivision, elevation above the surrounding regions produces modifications in the climatic character which are common to them all. It is impossible by the mere elevation above the sea to define the limits which entitle a place to be called a mountain health resort. Latitude and the features of the surrounding country exercise great influence in this respect, which manifests itself quite as much in the nature of the vegetation as in the meteorological character; and from both combined we may draw some inferences as to the probable physiological and therapeutic effects on the human constitution. In the low parts of Northern Europe, for instance, we find at an elevation of about 1200 to 1600 feet the vegetation peculiar to much

higher elevations in Southern Europe, unless the nearness of the sea or surrounding higher mountains exercise modifying influences. In latitudes nearer the equator a much higher elevation is required to produce analogous effects. Thus J. M. Toner says, "On Chimborazo the palms, bananas, and oranges grow at 5000 feet; at 10,000 feet, Indian corn and wheat; and at 15,000, barley and the more hardy grasses." In a rough way we may assume that in Northern Europe (above 50° lat.) an elevation of 1000 to 1500 feet produces a mountain climate, unless nearness of the sea or of higher mountains interfere; while in the centre of Europe (between 48° and 50° lat.), 1400 to 2500 feet are required; between 47° and 48°, 2400 to 3500 feet; and in the tropics 6000 to 9000 feet. The upper limits of elevation for health resorts likewise vary according to latitude and local circumstances.

We will begin our description with the *Swiss Alps.*

The general characteristics of the climate of the Swiss Alps in winter are: —

1. Low barometric pressure due to the altitude. 2. Great diathermancy of the atmosphere. 3. Low temperature. 4. Absence of fog and comparative rarity of cloud. 5. Low absolute and relative humidity. 6. Rareness of wind.

The patient is thus placed in an atmosphere of dry, still, cold, and rarefied air, and exposed to very powerful sunlight and sunheat.

What then are the effects of this climate upon the body? On arriving at one of the Alpine resorts the patient first experiences a certain amount of difficulty in breathing; any exertion causes him to pant; frequently he cannot sleep; sometimes there is headache; the bowels are often constipated, and there is a general feeling of listlessness; thirst and dryness of the throat are prominent symptoms. On examination the respirations are found to be quicker and the pulse accelerated. Marcet (54) has shown that the amount of carbonic acid and water exhaled by the lungs is increased. Acclimatisation may take from three or four days to as many weeks; when this is established the pulse will have fallen to its normal condition, the respiration will be fuller and deeper than on the plain (94), the bowels regular, sleeplessness gone, and appetite improved.

These effects are merely those of altitude, as they may be observed in the summer to the same degree, and quite as frequently as in the winter. In the winter we have further to consider the bracing effect of the dry, cold air. The influence which the cold air produces is probably seen chiefly in increasing appetite and digestion; at the same time an increased amount of water is exhaled by the lungs, and the exhalation of carbonic acid is promoted by the cold air of the Alps (Marcet). Taken altogether, it appears that altitude and cold combined produce a more rapid interchange in the tissues, and that in consequence of this greater activity the tissues acquire an increased resistance to the action of micro-organisms. The paramount constitutional benefit of climate in phthisis must lie in the increase of this resistance of the tissues, and such

is the unanimous opinion of all who have had much experience of the climates of high altitudes, and for these reasons: —

(*a*) Signs of constitutional improvement; gain in weight, and increase of appetite frequently precede any local improvement discernible by auscultation.

(*b*) Many patients, who have improved in the high altitudes, on going down to a lower level where the atmosphere may be equally pure and dry, begin to lose weight; while the disease shows signs of fresh activity.

This increased resistance seems to be brought about by the following factors: —

1. The large amount of time which is passed in the open air in a still atmosphere. 2. The tonic action of the dry cold air. 3. The purity of the atmosphere. 4. The large amount of sunlight. 5. Perhaps a general tonic influence exerted by rarefied air upon the metabolism of the body.

In past years much more importance was attached to the extreme rarity of phthisis among the natives of the high Alpine valleys. This rarity is rather to be explained by the outdoor life of the people, and the smallness of the communities; the absence or rarity of microbes is, however, well established.

The alleged fact that phthisis is unknown amongst the inhabitants of the steppes indicates that altitude may not be the only factor in conferring immunity; an outdoor life is at least as habitual to these people also.

Increased resistance is brought about not only by increased appetite, but also by improved digestion and assimilation. The patient finds, to his surprise, that he can eat a heavy meal without any subsequent lassitude and torpor. Viault and Egger have shown that there is a somewhat rapid increase in red corpuscles in patients taken to a high altitude. Further, Bert's experiments in Peru (9) prove that the blood at high altitudes takes in a much greater percentage of its volume of oxygen.

Besides the constitutional effects of the dry, cold, thin air, there are certain purely physical effects produced upon the lungs themselves. Owing to the rarefied atmosphere each breath taken must, to supply the due measure of oxygen, be deeper than on the plain. The effect of this is to enlarge the circumference of the chest; Williams (108) gives this enlargement at from one to three inches; other observers are inclined to put it at somewhat less, though all are agreed that it does occur [*vide* art. on "Artificial Aerotherapeutics"]. A further result of this deeper manner of breathing is thoroughly to open up all the air vesicles, and thus to prevent any accumulation of secretions in them. After a more prolonged residence at high altitudes a state is reached which has been termed "hypertrophy of the lung." The chest is enlarged to some extent and is hyper-resonant; the breath-sounds, instead of being weak, are puerile or exaggerated, but expiration is not prolonged. Whether this be merely a form of emphysema, or an actual increase in the

respiratory area of the lungs, we cannot say; but after considerable experience, both of the natives of the high Alpine valleys and of consumptive patients, we can assert that this condition is very rarely associated with the ordinary symptoms of emphysema.

The principal resorts are:—

Davos (5200 feet). Is less windy than the other resorts, but receives less sun during the day. It is adapted to a greater variety of cases, and the accommodation and nursing arrangements are excellent. It is connected with Zürich by rail.

St. Moritz (6000 feet). Is more windy than Davos, but has a slight advantage in the matter of sun. It is admirably suited to more vigorous cases, but severe cases are better at Davos. The accommodation is good.

Leysin (4712 feet). Above Aigle. Is well protected and receives a large share of sunlight. An admirably-conducted sanatorium has been established there, and thorough supervision of the patients is carried out.

Wiesen (4771 feet). Chiefly used as a halting-place to and from Davos.

Arosa (6100 feet). Admirably sheltered, and at the Kulm receives a fair share of sunlight.

Les Avants, above Montreux (3500 feet), may be of use where the higher elevations are ill borne. An equally sheltered and sunny establishment at an elevation of over 5000 is being built.

The elevated resorts of the *Rocky Mountains* have, of late years, come into repute, and, thanks to the admirable accounts given by Dr. C. T. Williams (107), and the earlier ones by Denison, their main features are becoming well known. These resorts are situated in the State of Colorado, on the eastern slopes of the chain as it traverses that territory, at altitudes of from 5000 to 7000 feet. Meteorological observations tend to show that the climate is somewhat drier than that of the Swiss Alps, and has a very distinct advantage in the matter of sunshine; at Colorado Springs during the winter the sun shines during the greater part of the day for 165 days out of 182 (77), and the mean temperature is higher than in the Swiss Alps, the snow only lying for a few days at most during the winter. On the other hand, there is very much more wind and much more dust than in Alpine resorts. Electrical manifestations are a prominent feature of the climate, but as to whether these influence the body for good or ill, we know, scientifically speaking, nothing. Their advantages are:—

1. Altitude, the effects of which we have already discussed. 2. Dryness. 3. Abundant sunshine.

The climate, although not possessing some of the advantages of the Swiss Alps, is better adapted on the whole for an all the year round residence; there is no snow-melting time, and the summer, although hotter, is more constant than in the Alps. Colorado, moreover, offers better facilities for employment, sport and exercise, than any other resort. Subjects of constitutional erethism will probably fare even

worse in Colorado than in the Swiss Alps. The accommodation is good, though, owing to the American fashion of meals, the food may not be so acceptable to the invalids as that of the Swiss hotels. It must be remembered also that the living expenses are heavier than in Europe.

The principal resorts are: —

Denver (5000 feet). A town of 150,000 inhabitants covering about five square miles. The mean annual temperature is 50°, the month of January showing a mean of 27·2°, and August 72·8°. Rainfall 14·17 inches (107). The accommodation is good, and the place presents all the advantages of a large town, though this can hardly be regarded as an unmixed benefit.

Colorado Springs (6022 feet). Seventy-five miles south of Denver; a town of 15,000 inhabitants. The mean temperature is 46·4°. Colorado Springs possesses an advantage over Denver in being almost exclusively a health resort, while the latter is a large commercial town.

Glenwood (5000 feet), on the Pacific slope, may also be mentioned; it possesses a most admirably-conducted hotel. The climate is, however, damper than that of the other slope.

New Mexico seems to possess a valuable winter climate, but is practically unavailable, owing to the absence of suitable accommodation which, even at El Paso, is far from good.

The Andes. — Another class of mountain climates, which may with advantage be touched on here, contains those of the Andes, since it was by experience gained in them that Archibald Smith was first enabled to draw attention to the benefit in the treatment of phthisis likely to be obtained by residence in elevated regions.

The main resorts are situated on the Pacific slope of the Andes — in Peru, and New Granada, at elevations varying from 8000 to 12,000 feet. The chief characteristics of these climates are: —

1. Moderate warmth even in the highest resorts, owing to their proximity to the equator. 2. Remarkable equability of temperature. At Jauja, according to Archibald Smith, during a whole year the temperature never rose above 60°, or fell below 50°. 3. Considerable atmospheric dryness. 4. Abundant sunshine.

We have thus a temperate and extremely equable climate, with the additional advantage of rarefaction of the atmosphere. The admirable results obtained there among the consumptive natives of the plain prove the curative properties of the climate. Unfortunately, however, at none of the resorts is the accommodation good enough for invalids. For English patients, also, the length of the journey is prohibitive, except in the case of vigorous men with limited disease. For such as these, and for arrested cases, who wish to have a settled home in a good climate, and who are willing to build their own houses, these resorts offer decided advantages. Dr. Smith points out that patients, as a rule, do better at an elevation of 8000 to 10,000 feet than at the higher levels.

The principal resorts are: —

Huancayo (10,000 feet), in Peru; the temperature of the whole year ranges between 51° and 63° (Williams).

Jauja, 10,000 feet, also in Peru, with a temperature ranging between 50° and 60° for the whole year round.

Quito, in Ecuador; a town of 80,000 inhabitants, situated at an altitude of 9500 feet, and with an all the year round temperature of about 60°.

Santa Fé de Bogota, in New Granada, at an elevation of 8648 feet. The temperature is 59°, and is fairly constant all the season through.

In *India* there are several hill-stations, situated in the Himalayas and Nilgiris; but, except for those who cannot leave India, they possess no particular advantages. The atmosphere is said to be very damp in the summer, owing to the heavy rainfall. The chief resorts are Simla (8000 feet) and Darjeeling (8000) in the Himalayas, with Ootacamund (7361) and Wellington (5840) in the Nilgiris. In considering the hill-stations of India we must bear in mind the nearness to the equator, by which the influences of altitude are considerably modified; and further, that the peninsula is surrounded, excepting at its broad base, by large masses of warm water. The periodical moisture-laden winds coming from these seas must, on reaching the colder mountain ranges, necessarily deposit a large portion of their humidity, rendering the soil damp, and the air emanating from it moist and impure.

Very different are the mountain climates on the north and north-west of the Himalayas, for the atmosphere on reaching them has lost a great part of its moisture on the southern slopes. Hence *Tibet* to the north, at 9000 to 11,000 feet, and *Cashmere* on the north-western chain, at 5000 to 6000 feet, possess healthy climates, and offer sites for most useful health resorts.

A class of resorts of moderate altitude (about 1700 feet), presenting peculiarities worthy of notice, are *Görbersdorf* in Silesia, *Falkenstein* in the Taunus, *Reiboldsgrün* (2250 feet) in the Erzgebirge, and *Hohenhonnef* in Rhenish Prussia. These resorts base their efficacy not so much upon their climate as upon the manner in which, by careful management and artificial shelters, an open-air life is rendered possible to the consumptive, even in a somewhat inferior climate. Further, the patients reside in sanatoria, in which every, even the smallest, detail of their daily life is under the immediate control of the physician, while obedience to his orders is a condition of residence. This system of treatment was inaugurated by Dr. Brehmer at Görbersdorf some forty years ago; his main contention being that the essential point in the cure of phthisis was supervision of the minutest particulars of the patient's life, aided by drugs and hydrotherapy when necessary. The soundness of his views has been abundantly proved by the high percentage of cures amongst his cases, while to his teaching is due the sytematisation of the mode of life at Davos and other health resorts. We cannot help remarking here that Brehmer's results, obtained in an inferior climate, are better

than most of those obtained in far more suitable localities, where the old haphazard traditions of treatment still reign. The difficulties of establishing such a system amongst English patients are great; but some modified form of Brehmer's system could easily be brought into vogue by a determined effort on the part of the medical profession. We have yet much to learn from the German physicians as to the best possible method of utilising each climate. Brehmer's system is carried out at the establishment which he founded at Görbersdorf, situated in a pine-clad valley in Silesia, at an elevation of 1700 feet. Dr. Dettweiler, one of Brehmer's assistants, and Dr. Hess now direct the establishment of Falkenstein, situated in a sheltered valley of the Taunus, at an elevation of 1500 feet; to this is now attached a sanatorium of 100 beds for patients of small means. Dr. Meissen, another former assistant of Dr. Dettweiler, directs yet another sanatorium at Hohenhonnef, about 1600 feet high. Dr. Trudeau, again, carries out a system similar to Brehmer's at his sanatorium in the Adirondacks, in the United States of America; here the patients lie during the greater part of the day in open verandahs, even in a temperature of 10° below zero.

The large number of excellent hotels in the mountainous part of Switzerland, Italy, and France, at elevations of about 5000 to 6000 feet, may be ascertained from the current guidebooks.

The *Eastern Alps*, with the Dolomites and the Tyrol, contain many beautiful localities which are gradually being provided with hotels suitable for delicate persons. In the *Dolomites* we may specially mention *Campiglio* (Madonna di San Campiglio), *San Martino di Castrozza*, *Schluderbach*, *Landro* or *Höhlenthal*, and *Cortina d'Ampezzo*. In the *Tyrol*, *St. Gertrud*, in the Sulden Valley, is above 6000 feet, all the others are below 5000, and the majority below 4000, descending to about 2000: the *Mendelhof*, near Botzen; the hotels on the *Semmering Pass; Gossenap*, near the Brenner Pass; *Innigen*, *Niederdorf*, *Toblach*, and *Neu Toblach*, in the Puster Valley; *Kreuth* and the *Achensee; Oberstdorf; Berchtesgaden*, with *Steinhaus* and *Vordereck; Zell am See; Partenkirchen* and *Kainzenbad; Aussee* and *Altaussee; Innsbruck*, with *Igls*.

There are, besides, many even less elevated localities, which, owing to the beauty of the situation and the comfort of the hotels, may be selected for shorter or longer stays, such as *Reichenhall*, *Salzburg*, *Ischl*, *Gmunden*.

Italian Mountain Stations. — The mountain ranges of *Italy*, excepting the southern valleys of the Alps, included in the Alpine resorts (*Macugnaga*, *Gresoney*, *Alagna*), do not yet offer many localities which have adequate accommodation. *Ceresola Reale* in Piedmont, 5100 feet high, and *Abetone* and *Serrabassa* in the Apennines, at an elevation of about 5000 feet, deserve to be mentioned; and at lesser elevations, *St. Martin Lantosque* and the *Certosa di Val Pesio*, in the Maritime Alps. *Perugia* and *Siena* are scarcely elevated enough to be regarded as hill stations, but they are delightful in spring and autumn.

In the *Pyrenees* we have the different spas, which can also be used as climatic health resorts — *Barèges, Cauterez, Bagnères de Luchon, Bagnères de Bigorre, Eaux Bonnes,* etc., but they are less bracing than many of the Alpine localities.

In the mountains of the Auvergne *Mont Dore* has a claim to be regarded as a mountain health resort, but widely useful accommodation in this district might be provided on the *Puy-de-Dôme,* near Royat.

The health resorts of the *Black Forest* are of lesser elevation than those of Switzerland, but exercise, nevertheless, a moderately bracing though less stimulating influence. In addition to elevation, most of these localities have in their neighbourhood large pine forests, which exercise a purifying and equalising action. *Höchenschwand* and *Schönwald* are the only places worth mentioning above 3000 feet; the other available localities are between 3000 and 1400 — *Schluchsee, Titissee, St. Blasien, Triberg, Freudenstadt, Allerheiligen, Rippoldsau, Griesbach, Badenweiler.*

Rather similar in character are some localities in the Vosges Mountains, of which *Hohwald, Dreiaehren,* and *Odilienberg* are the best known.

Besides *Görbersdorf* and *Reiboldsgrün, Falkenstein,* and *Hohenhonnef,* already mentioned as sanatoria for the treatment of consumption, the eastern mountain ranges of Germany are rich in well-wooded health resorts of local fame, ranging from 1500 to 2500 feet.

The *Harz* Mountains in the north of Germany offer many useful summer resorts between 1400 and nearly 3000, especially *Clausthal, Andreasberg, Alexisbad,* and *Harzburg;* the two first are already in use as sanatoria for phthisis all the year round.

The mountains and elevated places of *Great Britain* differ in climatic characters from those on the Continent. The atmosphere is more humid, less transparent and transcalent, the sun heat is less high, the temperature is more equable. There are scarcely any health resorts higher than 1000 feet, but the climate at such and at lower elevations is much more bracing than at similar elevations on the Continent. This is owing partly to the greater coolness of the summer, partly to the absence of high mountains around them, preventing free access of air. There are no elevated winter resorts. The air on the Scotch and Yorkshire moors is thoroughly invigorating, but, unfortunately, the owners do not as yet tolerate hotels or sanatoria on them. There is, however, a considerable choice of localities, with good climates and fair accommodation. In Scotland — *Braemar, Ballater, Grantown, Forres, Strathpeffer, Blair Athole, Pitlochrie, Inversnaid,* the *Trossachs, Crieff,* and *Moffat.* In England — *Buxton, Harrogate, Ilkley, Gilsland, Malvern, Tunbridge Wells,* and *Frant.* In Wales, *Llanberis* and *Llandrindod* are best suited for those who want some comfort with mountain air. It is much to be regretted that there are no good inns higher up on the mountains. In the south of England Hind Head and Black Down have the advantage of good villas, but not of hotels; and the same is the case with the chain of Leith Hill. On Dartmoor moderate accommodation is to be found at Princetown, about 1400 feet high.

South Africa. — The district of South Africa which offers several localities possessing a climate suitable to invalids, is the Karroo, a rolling heath-like country, varying in elevation from 2500 feet to 6000 feet. It is divided by the Nieuweld Mountains into two districts, Central and Upper Karroo. Of these the former slopes gradually southward, while the latter stretches northward as far as the Orange River. The climate is characterised by extreme dryness of the atmosphere, great heat in the summer, and small rainfall. The winter nights are cold, but, according to Dr. Saunders, the days are bright and sunny. The advantages of this climate are its altitude and the abundant opportunities it offers for outdoor life, without danger of taking cold; its drawbacks are the large amount of dust and the extreme heat of summer, though, owing to the dryness, the latter is not severely felt. The climate is bracing, but too exciting for persons of a nervous temperament. In timing the arrival of patients it must always be remembered that the seasons are the reverse of our own. The simple character of the accommodation, moreover, should deter the fastidious and any invalid not possessed of a fair amount of constitutional vigour.

Of the resorts whose capabilities have been so admirably summarised by Dr. Symes Thompson (89), we may mention —

1. In the Great Karroo: Craddock (2855 feet) and Beaufort West (2792 feet).

2. In the Upper Karroo: Burgersdorp (4552 feet) and Tarkastad (4280), at which good results have been obtained in the treatment of phthisis; also the flourishing townships of Aliwal North (4348), Kimberley (4012), and Bloemfontein (4500). Pretoria in the South African Republic is also rising into favour as a health resort. Ceres (1493), with its sanatorium, and Grahamstown (1800), form excellent intermediate stations between the coast and higher altitude sanatoria.

Australia. — The regions of Australia, possessing climates suitable to invalids, are the inland plains, certain localities in the Blue Mountains and the Australian Alps. The climate of the coast region, in which all the chief towns are situated, is too variable, owing to the cold southerly winds and the hot winds which blow from the central desert. The mountains, which fringe the coast from the South Australian border to Queensland have in the main a temperate, dry and bracing climate. Although amongst the varieties of their climates there are probably some which would be of great value, yet the want of accommodation, except at two or three places, materially lessens their utility. The available resorts are confined to those on *Mount Macedon* in Victoria, with *Catoomba* and *Mount Victoria* in New South Wales. The former, situated 44 miles from Melbourne, consists of Upper (3000 feet) and Lower Macedon (1660 feet), with the excellent sanatorium, *Braemar Wood End* (2500 feet). The mean annual temperature of *Macedon* is 53° F. The locality forms a good place of sojourn for those spending a short time in the colony (8).

Mount Victoria (3490 feet), 77 miles from Sydney, mean annual

temperature 53° F., provides an excellent change from the climate of the inland plains.

Catoomba (3349 feet) is slightly more humid than the last named.

The chief characteristics of the Inland Plains are extreme dryness of the atmosphere, abundant sunshine, and small rainfall. All these conditions mean ample opportunities for outdoor life. The drawbacks to the climate are the large amount of dust, the occasional occurrence of a hot north wind, and the possibility of a drought. The climate is undoubtedly bracing, the danger of chills is slight, and there are no marked ill effects upon the nervous system, such as sleeplessness, etc.

The Inland Plains divide themselves into two districts: the Riverina in Victoria, lying to the north of the Murray River, and the Darling Downs in Queensland, an upland plateau (2000 feet) lying to the east of the former.

According to Dr. Lindsay (47) the heat in summer in the *Riverina* is considerable, though easily borne. In winter there are slight frosts, but the days are warm. The *Darling Downs* are somewhat cooler and less exposed to the hot wind. In both districts the accommodation is rough, and the climate is best enjoyed by residence on a station.

For some cases of phthisis the climate is admirably suited; the patient, however, must possess a good share of constitutional vigour, and must be ready and willing to content himself with the monotonous fare of a station or up-country township. Accommodation can be obtained at Deniliquin in the Riverina, and Warwick and Towoomba in the Darling Downs.

II. The Lowland Climates. — After having considered so many regions under the heads of Marine and of Mountain Climates, we can throw but a rapid glance at some of lower regions not included in the former. Our foremost attention is claimed by Egypt.

Egypt owes its virtue as a climate chiefly to its being composed mainly of desert, so much so that the fertile spots included in the wastes share, on the whole, the characteristics of the desert air. The main characteristics of the climate are: —

1. *Warmth*, the mean temperature at Cairo for the winter months being 58·3°. 2. *Large Daily Range*, the difference between day and night temperatures varying from 35° to 19°. 3. *Low Relative Humidity*. 4. *Abundant Sunshine*. — Blue sky was chronicled on all but fifteen days during five months at Assouan, in the winter of 1892–93 (Longmore). 5. *Small Rainfall*. — Six rainy days only in five months were chronicled at Assouan in 1892–93. 6. The extremely aseptic character of the air, which is constantly refreshed by a breeze blowing over hundreds of miles of desert whence no emanations rise.

Most of the observations have been taken in localities situated on the cultivated land. Dr. Canney's observations, however (supported by Dr. Longmore's personal communications), taken in the desert at Luxor, and in other situations in Egypt, tend to show that the climate in the desert itself has a smaller daily range (17° in Luxor

desert as against 32° in Luxor) and a lower relative humidity (54° in Luxor desert as against 69° in Luxor). The advantages of the climate are dry, warm, sunny days with cool nights, and a marvellously pure atmosphere. The drawbacks to the climate are the not infrequent presence of cold winds (though not to the same extent as on the Riviera), and the occasional occurrence of hot winds laden with dust; these are not only constitutionally most depressing, but intensely irritating to the lungs.

The physiological effects of the climate may be described as bracing to the organism as a whole, and sedative to the nervous system. Dr. Sandwith (70) gives records of 105 cases of phthisis; improvement took place in 72.

In Egypt the invalid can spend the greater part of the day in a warm climate, while at the same time sleep is encouraged rather than interfered with, and the nervous system is soothed. The danger of chill at sunset is, however, always present, and has to be guarded against as carefully as on the Riviera. The length of the journey and the great expenses of living necessarily exclude a certain number of invalids.

The chief individual resorts to be considered are: —

Cairo. — This should be avoided, as it is a crowded town, offering too many social temptations. Although the sanitation and water-supply of the hotels are good, the town itself is far from being in a sanitary condition.

Helouan. — About 15 miles from Cairo, standing in an oasis in the desert. There is more wind than at some other resorts; the accommodation is excellent. As it is a little above the level of the Delta Helouan can be utilised also from November to January.

Mena House. — Near the pyramids, an admirably kept hotel. The climate in the late winter and early spring is much the same as that of Helouan. Owing to its proximity to the Delta the best season to visit Mena House is from the middle of February onwards; before that date there is too much moisture in the air, owing to the drying up of the inundated plain.

The Nile Voyage. — This may be made in two ways: (*a*) by steamboat, (*b*) by dahabeyah. (*a*) The steamboat voyage is shorter, but less repose is obtained than on the dahabeyah. There is, moreover, far too much wind for serious invalids, and often a difference of 10° between different parts of the boat, and much more between sun and shade. Patients suffering from the throat often catch cold and become feverish. Here, too, the belief prevails that climate must do everything, and that the doctor need not be consulted. The long and hurried excursions to tombs and temples afford another source of danger to many invalids. Dr. Longmore, as the result of his experience, is inclined to regard the voyage during the months of January and February as unsuitable to the pulmonary invalid, particularly so far as lower Egypt is concerned.

(*b*) The dahabeyah, on the other hand, affords perfect leisure, while the contrasts of temperature are not so great. It is, however, costly, and the patient, unless he can afford a travelling physician, will be

away from medical supervision; even in promising cases this is rarely advisable. During the months of January and February the dahabeyah should be kept south of Luxor (Longmore).

Luxor, situated on the Nile, 450 miles south of Cairo, possesses a milder climate than lower Egypt, being warmer and not so subject to cold winds. Luxor is admirably suited as a residence for the invalid from the end of November to the middle of March. Moreover, the invalid can travel by train within a day's boat journey of Luxor; this is a great boon to those arriving late in the season, for whom the boat voyage is unsuitable.

There is an admirable site for a sanatorium south of the hills above the tombs of the kings. Here, owing to the conformation of the country, the full advantage of desert air could be enjoyed to a greater degree than in any of the present resorts.

Assouan stands at the first cataract; it is somewhat more bracing, drier, and warmer, but, on the whole, a little more windy than Luxor. The accommodation is fair in the new hotel, but there are few arrangements for sitting in the open air without exposure to draughts and dust. This, however, we hear is to be remedied, and with judicious management Assouan can be made an excellent resort for sufferers from rheumatism, early phthisis, and the like.

On the whole the great advantages of desert air are not yet sufficiently available. We may say, however, that our experience of treatment by continued residence during several entire years in the Nubian Desert, under tents shifted from one place to another, has, in several advanced cases of consumption, given results which are altogether superior to any obtained from any health resort or from any other treatment. Yet if, at the site indicated near Luxor, a hotel were constructed on an improved plan as regards ventilation, air spaces for the night, food, and so forth, the conditions, to judge from the medical and scientific observations that have been made on the climate, would be nearly perfect.

Pau, in the south-west of France, about 630 feet above sea-level, owes the peculiarities of its climate to its situation north of the Pyrenees, not far removed from the Atlantic, and to its being surrounded by a wide circle of hills. Thus it enjoys considerable calmness of atmosphere with the exception of occasional storms. The air is less dry, and the number of rainy days is greater than at the Riviera. The mean temperature from November to April is about 48·5° F. which is nearly 5° F. less than at the Western Riviera resorts, but it is rather more equable. There is less sunshine and sun heat; the difference between sun and shade, and between day and night is less. On the whole the climate may be called sedative, and is therefore more suitable to cases with an irritable mucous membrane and an irritable nervous system than the Riviera (85).

Dax, in the south-west of France, has a somewhat similar climate, but is less sheltered and more under the influence of the Atlantic.

Arcachon, which has been mentioned under the marine climates, but

has almost equal right to a place here, has some points in common with Pau.

The interior of Italy is rich in delightful localities, which may temporarily serve as residences to invalids, but few of them can be regarded as health resorts.

Rome will always claim the attention of physicians called upon to advise on climates, although it has long lost its great reputation in the cure of phthisis. November is often rainy; December, January, and February are frequently cold; but March, April, and part of May are mostly pleasant, and may be useful in cases of arrested phthisis, cases with chronic bronchial catarrh, chronic rheumatism, gout, and mental depression, provided due care be taken to avoid over-fatigue in sight-seeing, and changes from the hot sun into cold galleries and churches. The climate of Rome should not be called relaxing, it may be said to take an intermediate place between Pau and the Riviera. Dr. Charles and other physicians residing in Rome describe the hygienic condition as much improved, especially in consequence of the excellent water-supply.

In the north of Italy the Lake district offers some climatic advantages, especially the *Lago Maggiore*, the lakes of *Como*, *Varese*, and *Lugano*, and the *Lago di Garda*. The climates of the different localities on these lakes are by no means the same, but all have in common the position to the south of the sheltering Alps, and the influence of the large sheets of water near which they are situated. They offer less warmth, less shelter, and less sun than the Riviera, and have more rain; but, compared with England, the number of clear days is greater and the relative humidity is smaller. The late Dr. Scharrenbroich, in a carefully-written work on *Pallanza*, gives the relative humidity as 67·6° F., the number of bright days during the colder seasons 185, of rainy 61. Pallanza, which is open throughout the year, has a mean winter temperature of only 39·1° F., which is scarcely more than the inland localities in the south of England, but in spring 54·4°, in summer 71·4°, in autumn 55·65°. The climate may be regarded as moderately dry and stimulating. That of *Locarno*, likewise open in winter, is somewhat similar. *Stresa* and *Baveno* are rather less sheltered, and are suitable only for spring, summer, and early autumn. On the Lake of Como, the *Villa d'Este*, *Menaggio*, *Cadenabbia*, and *Bellagio* are favourite resorts in spring and autumn. *Lugano* in winter and spring, according to Dr. Thomas, is slightly cooler than Pallanza. *Varese*, on the lake of the same name, deserves likewise to be mentioned; it lies higher (1250 feet) than the localities on the four other lakes, which lie between 600 and 1000 feet. The accommodation at *Orta*, with its beautiful little lake, is not yet quite so good as at the other places mentioned.

The *Lago di Garda*, south-east of the Lake district mentioned, at the foot of a precipitous mountain range, possesses a much more sheltered tract of shore than any of the other Italian lakes. It offers a very remarkable instance of the power of configuration, by which a limited

Riviera-like climate is produced: here many delicate plants grow in the open air, and even lemon-trees on steep terraces. At a village, called *Gardone-Riviera*, a winter resort has sprung up which offers many advantages to those requiring much shelter.

Arco, which has fair, though not the same amount of shelter, lies very near to the Lago di Garda, in an easterly direction; it has for many years been used as a winter resort. All these localities are less dry, less warm, and less stimulating than the Italian Riviera, but less sedative than Pau.

We may here allude to two other localities, which have in former years enjoyed a wide reputation, especially in the treatment of phthisis, viz., *Meran* with *Obermais*, and *Botzen* with *Gries*, both at the southern slopes of the Tyrolese Alps. They have bright, sunny climates, with a certain amount of shelter and moderate relative humidity.

Third Section. — Utilisation of Climates

We cannot regard climatic treatment in the narrow sense of treatment by the mere physical elements of climate, but we must include in it and avail ourselves of all the agencies associated or associable with the change of climate. Some of these agencies act principally on the bodily functions, while others bear directly on the mental functions, and through them on the organs and tissues.

Physicians who are consulted about the choice of a climate often meet with misconceptions on the part of the patients. The latter not rarely think that it is sufficient to know that they have "gout," or "dyspepsia," or "rheumatism," to enable the physician to recommend the "best climates" for those complaints: they do not consider that "gout" is often complicated with other affections, and differs so widely in different persons and constitutions, as to need widely different treatment; and that the same is the case with "dyspepsia," with "rheumatism," and with almost all other complaints. The patient, moreover, frequently regards the "climate of a place" as a fixed agent, comparable to a fixed dose of a particular drug, — say a grain of calomel, or three grains of quinine, or five of iodide of potassium, — while in reality the climate of a place during a certain season, say winter or spring, is an unstable agent, varying with the weather. Some physicians are in the habit of saying that all climates are uncertain with the exception of Egypt, but after the personal experience of a winter in Egypt we cannot allow even this exception.

To answer a question frequently asked, *What is a good climate?* our answer is: A good climate is that in which all the organs and tissues of the body are kept evenly at work in alternation with rest. A climate with constant moderate variations in its principal factors is the best for the maintenance of health. It calls forth the energy of the different organs and functions, their power of adaptation and resistance, and keeps them in working condition. Such are the climates of England

all the year round, and they belong to the most health-giving in the world. They produce the finest trees, the finest animals, the finest men, and are most conducive to longevity. They are, it is true, not the most agreeable or exhilarating climates; but the brightest and most exhilarating climates — such as those of Egypt, Spain, Italy, Greece, Asia Minor — are not the best for health and longevity; they are in many respects very inferior to those of England.

The best climates, however, for healthful development and for maintenance of health need not be the best, may even be injurious to delicate or diseased persons whose organs and tissues have, temporarily or permanently, lost their energy and their power of resistance and adaptation. We must, therefore, endeavour to find *climates for invalids*. And here we must say at once there are no perfect climates for invalids. Relatively good climates for a given case are those in which the influences injurious to this case are either absent, or prevail only in a much less degree; and where at the same time other influences exist which, when properly utilised, effect a general improvement of the whole constitution, and thus facilitate the recovery of the diseased or weakened organs and tissues, as far as possible. Pure air and water, the possibility of spending a great part of the day in the open air, good hygienic and dietetic arrangements, and the presence of a good local physician conversant with the peculiarities of the climate and of the entire locality, are the most necessary conditions.

The physician is, indeed, a very important part of a health resort and of a climatic cure, although the invalid is often disinclined to see this. Many lives are needlessly lost by trusting to the climate alone. The exhilarating influences of a climate, the many interesting objects of a place and its neighbourhood, and the social entertainments, are sources of temptation, lead often to undo exposure, to over-exertion, or to chills, and may destroy the chances of recovery for ever; on the other hand, with the help of a judicious physician, not only may the dangers resulting from the defects of a place be escaped, but these very circumstances may also be employed to the benefit of the invalid.

The invalid must begin by studying, with the guidance of his physician, the following essential points: —

(1) The selection and arrangement of his rooms for air and sun, and other hygienic influences. (2) The arrangement of his meals as to quality, quantity and time. (3) How to be as much as possible in the open air. (4) What kind and amount of exercise to take, and at what times of the day, and when to rest. (5) How to clothe himself at different times of the day and of the season. (6) How to manage the skin. (7) How to occupy the mind.

Without due attention to these points many cases, even at the best resorts, are not benefited; with it, good results can be obtained even at inferior localities.

In former times climatic treatment was almost limited to diseases of the respiratory organs, but at present we know that the treatment of

almost every chronic deviation from health may be assisted by judicious change of climate. Our survey of the principal conditions in which climatic treatment is usually resorted to must, however, be a summary one.

The Treatment of Phthisis by Climate. — The utilisation of climate for the alleviation or arrest of phthisis is perhaps the most important office which change of air can fulfil. From its very nature it is only within the reach of the richer of the victims of this malady. Too often, moreover, the change, either owing to the relentless march of the disease, the unsuitable locality selected, or indeed, and more commonly, the imprudence of the patient himself, ends in disappointed hopes. The selection of a locality is often one of the most difficult problems with which the physician is confronted. Accumulated clinical experience, it is true, has given us a series of fairly definite indications to guide us in the choice; more frequently than not, however, we have to be governed in our selection by the poverty of the patient; and, instead of the best possible climate, have rather to consider where he may find an opportunity of earning a livelihood.

The cases which will receive most benefit from a stay in the *Swiss Alps* require somewhat careful selection. Early cases of either unilateral or bilateral phthisis in young and fairly vigorous persons, in which the disease is of a limited character and the pyrexia moderate, should be sent to the Swiss Alps in preference to any other resort. In young persons a sojourn of one or two years in the Alps will probably not only arrest the disease, but so establish the constitution that the patient may cautiously resume his ordinary occupation at home. It has been urged that these cases will do well anywhere; but not only do statistics show that more first stage cases are arrested in the Swiss Alps than elsewhere, but the experience of all those who have compared cases coming from various resorts testifies in favour of the greater quickness and certainty of the cure in the Swiss Alps.

In the early days of high altitude treatment a history of hæmoptysis was looked upon as a bar to the employment of the climate; the reasons for this belief were mainly theoretical, and a more extended experience has shown that the very reverse is the fact, and that the hæmorrhagic cases do particularly well there.

When a case has passed on to the stage of excavation, although the ultimate outlook may be, on the whole, less hopeful, clinical experience warrants us in saying that a greater benefit may be anticipated from a prolonged or indeed an indefinite sojourn in the Alps than from any other form of climatic treatment. The presence even of considerable pyrexia, so long as we can be sure that it arises rather from septic absorption than from active tuberculosis, forms no bar to sending the patient away. In the bronchiectatic form of phthisis progress is certain to be extremely slow. Since, however, the majority of these cases arise directly from a pleuritic effusion, we should take early advantage of the very definite influence for good which the rarefied air is likely to exert upon collapsed lung; at the same time we shall put the whole constitution in a better

condition to withstand the inevitable strain which following years will bring. In this form of disease a constantly high bodily temperature, or occasional rushes of temperature up to a great height, form no impediment to sending the case to the Alps.

A further class of cases which should, except in the face of obvious contra-indications, be so treated, is that in which the phthisis supervenes after a pleuritic effusion in a young subject. From the climate of the Alps, in such cases, we may almost always anticipate the happiest results due not only to the expansion of the compressed lung, but to the strengthening of a constitution of whose proneness to tubercle the effusion was but a manifestation.

What are then the *symptoms or conditions which contra-indicate the High Alps* in cases of phthisis? We will consider first the more distinct and absolute of these.

The presence of albuminuria forms an absolute contra-indication. Any affection of the kidneys bars the employment of the climate of the Alps; such cases are invariably aggravated.

Cases in which there is valvular disease of the heart or degeneration of the arteries should never, except under very exceptional circumstances, seek the climate of the Alps; indeed this rule is absolute as regards the condition of the arteries. In those rare cases of affection of the mitral valve in which the compensation is thoroughly good the patient may be sent without much hesitation. In disease of the aortic valves the experiment is a more hazardous one, and we should be very well assured that compensation is perfect before sending the case to high elevations.

The next complication which would contra-indicate the Alpine climate is the presence of diarrhœa due to tubercular ulceration; diarrhœa of a merely catarrhal nature may, however, derive benefit from the climate. As regards laryngeal complications when, as is commonly the case, there is slight hoarseness with the laryngoscopic appearances of laryngeal catarrh, even though the appearances are such that tubercle cannot be definitely excluded, the patient may be sent. Where there is a tubercular ulcer on one vocal cord, provided that the arytenoids are free, he may also seek the Alpine air, appropriate treatment being at the same time applied to the throat. When, however, the arytenoids are involved, or when perichondritis is present, the case should on no account be sent thither.

When there is high fever due to the rapid extension of the tubercular process in the lungs the Alps must be forbidden; but if the fever yield to treatment and the inflammatory process lessen in intensity, the question may be reconsidered. In cases where the disease is far advanced, and the amount of diseased lung large, the Alpine air should not be tried; the respiratory area will probably be insufficient to meet the added strain, and the fatal event will be hastened. The subjects of constitutional erethism — persons, that is, with habitually quick pulse, subject to feverish attacks, and with an irritable condition of the nervous system — almost invariably get worse rather than better in the rarefied air.

There are, besides, a certain number of persons who cannot bear cold; elderly persons especially, in spite of the hot sun, are injuriously affected by the cold air of the Alps. The exclusion of such cases from the Alpine treatment is often a matter of difficulty. It is rarely safe to place much faith in the patient's statement that he cannot bear cold; but such a statement should ensure a careful estimate of his constitutional vigour.

The length of residence in the High Alps which is likely to secure restoration to health must necessarily vary with the progress of the case. We should never, however, lead the patient to expect thorough restoration to health from a residence of less than two winters. This term has often to be cut down for pecuniary reasons, but it should never be shortened in deference to the wishes of the patient. If the case progress favourably the patient will probably have got most of the benefit he is likely to obtain from the treatment at the end of two years. There are always a certain number of persons, however, who relapse if long away from the high altitudes. For these there is nothing for it but to settle for the winter, at all events, at one of the Alpine health resorts. A late distinguished man of letters was a remarkable instance of a life so spent, and literature is the richer for his courage and prudence.

A point upon which the local physicians justly lay great stress, is that the residence should be continuous; that is, two winters and one summer at least should be spent in the High Alps. It has been the custom for invalids to go down to a lower level during the snow-melting time in the spring. Latterly, however, the physicians only allow patients who are doing well to do this, and rather to provide a change of scene than for other reasons. A critical case is likely to lose more by the journey to and fro than by remaining during the few damp days. The places most usually resorted to in the spring are Ragatz and Thusis. Sometimes a descent to the Italian lakes or Montreux is permissible in the autumn.

The Alpine sanatoria, Davos and St. Moritz particularly, owe not a little of their success to the very thorough and efficient manner in which every detail of the patient's life is supervised by the local physicians, as contrasted with the somewhat haphazard method only too much in vogue at other health resorts. The opportunities for over-indulgence in violent outdoor sports which these places offer, and the temptations in large hotels to an irregular way of living, are in most cases controlled by the physicians.

The time of year at which the patients should be sent is a matter of some importance: the end of September is the best time, since the patient then becomes acclimatised before the winter sets in. Often, however, the patient falls ill later in the year. It is a sound rule not in any case to send a patient after the end of January; he will then get but little benefit before the snow begins to melt, and it would probably be better to wait until June. In a doubtful case it is better to make the ascent gradually, stopping a few days at a moderate elevation.

During the summer in the Alps the invalid can find change of scene at a like elevation at Pontresina, Maloja, and other localities.

The special utility of the *Colorado* resorts lies in the fact that profitable occupation, or at least a livelihood, can be obtained in a climate little if at all inferior to that of the Swiss Alps. The expanse of country possessing, with very minor modifications, a uniform climate is large; while one of the resorts, Denver, is a great city with flourishing industries. In the selection of cases for treatment in Colorado the same contra-indications hold as in the case of the Swiss Alps; we should, however, be more rigorous in excluding doubtful cases, seeing that the experiment entails long journeys by sea and land.

Some persons, indeed, with a limited area of damaged lung, who find the Alpine climate too cold, may seek the equally elevated yet warmer climate of Colorado, with better prospects of recovery than would be given by a descent to a lower level. Moreover, Colorado presents advantages to that class of cases to which we have before referred — those cases, namely, which remain quiescent in the mountains, but relapse in the plains. Young subjects, the children of phthisical parents, not themselves tubercular, but for whom a change of climate is thought advisable as a prophylactic measure, — as, for instance, after a pleural effusion, — will do better in Colorado than elsewhere.

The cases which are likely to receive benefit from *Australia* are: — 1. *Cases of early consolidation, in which there is no fever.* 2. *Quiescent cavity cases.*

In every case there must be a sufficient amount of constitutional vigour to support an outdoor life, and all the more serious complications — laryngitis, intestinal ulceration, or high fever — are absolute contra-indications. With regard to employment, we must point out that a sedentary occupation followed in one of the coast towns holds out no prospect of cure; for such cases the highland townships of South Africa or Colorado would offer greater advantages.

With regard to *South Africa*, the same rules as to choice of cases hold good. Practically, unless the patient have plenty of vigour, and there seems solid ground to hope for early subsidence of the disease, he had much better seek some climate nearer home. Hæmoptysis occurring early in the course of the disease is no bar; late hæmoptysis proceeding from a cavity is an absolute bar.

The advantage of the *Egyptian* climate in the treatment of phthisis lies in the warm, sunny days, the dryness of the atmosphere, and the aseptic character of the air. Its drawbacks are: the short time of year during which it is available, and the danger of contracting chills, chiefly abdominal. The cases of phthisis most likely to derive benefit from it are: — (*a*) Cases complicated by bronchitis in which emphysema is also present. (*b*) Cases of bronchiectatic phthisis, for which a winter or two in the Alps have already been prescribed, will often derive great benefit from Egypt. (*c*) Cases for which the Riviera is too cold, or in which chills often recur. (*d*) Cases of early consolidation in which, either owing to susceptibility to cold or some other reason, the Alps are contra-indicated. (*e*) Cases with albuminuria in which the destruction of lungs

is not very great. (*f*) Cases in which insomnia and nervous irritability form prominent symptoms.

On the other hand we are not justified in sending cases presenting the following complications:—

1. *Intestinal Ulceration*, or indeed any tendency to diarrhœa whatever. This is sure to be aggravated. 2. *Laryngeal Ulceration*. The dryness of the air always aggravates the symptoms. 3. Cases beginning with acute pneumonic symptoms. These should not be sent on account of the length of the journey and the short time during which the climate is available.

The main virtues of the *Riviera climate* are that it permits the patient to pass several hours of most days in a fairly warm and dry atmosphere which, owing to the vicinity of the sea and mountains, is comparatively free from impurities. Its drawbacks are the winds which materially curtail the amount of open-air life, and the danger of chills from the contrast of sun and shade temperature. Early cases, as a rule, will do better in the Alps, but there always remains a residuum for whom the Riviera will be the most appropriate climate. Patients for whom the Alps are too cold will generally do very well on the Riviera without going so far afield as Egypt, while the more bracing climate will increase the resistance of the body more than will that of Madeira. Some persons, after one or two winters passed in the Alps, find that they do not stand the cold so well as at first; such persons will generally continue to improve on the Riviera. A continuous residence in the Alps sometimes also impairs the appetite; this symptom will generally be removed, and the general condition of the patient ameliorated, by a change to the Mediterranean.

When the time of the year at which the disease manifests itself is too late to admit of the possibility of Alpine treatment, the spring may with advantage be passed on the Riviera.

Phthisical patients, in whom the disease is characterised by a great deal of irritation, as evidenced by signs of catarrhal pneumonia, probably do better on the Mediterranean coast than elsewhere. This form of phthisis frequently follows influenza, and such cases generally do well. When the bronchitic element is marked the Riviera will often be found practically as efficacious as Egypt, and is nearer and less expensive.

Cases of laryngeal phthisis often improve under appropriate treatment at Mentone and San Remo. Even in the more advanced cases patients may be sent, if willing to take the risk; for though there may be but slight hope of recovery, yet their life will, on the whole, be easier than in England. They must, however, be pecuniarily in a position to afford every possible comfort.

Amongst the serious drawbacks of the Riviera must be mentioned the numerous social temptations. The Riviera has become the favourite resort of healthy and wealthy people who crave for excitement and amusement, the charms of which are irresistible to their invalid friends, who not rarely lose through them the last chance of recovery. The danger is much aggravated by the mischievous habit amongst patients

at the Riviera, not to place themselves under the entire guidance of a physician, not to consult him at the beginning and during the whole stay about the manner of living, — hygienic, dietetic and social, — but to act as it pleases themselves and their healthy friends, and to fly to the doctor only when acutely ill. The climate itself would offer very good chances to a great many consumptive patients if they were placed in well-arranged sanatoria, or at all events under strict medical guidance; but the present fashions render this almost impossible.

Madeira is often more useful in consumptive cases with much irritability of constitution, and especially of the mucous membranes, accompanied by a dry cough; and in cases complicated with emphysema. It deserves a trial also in patients with laryngeal irritation. Patients with much expectoration, or with a weak intestinal mucous membrane, ought not to be sent to Madeira.

The *Canaries* have a wider range of usefulness than Madeira; they are less humid, and the principal localities offer more chance for exercise on level or gently-rising ground. Life there is, unfortunately, very monotonous.

Pau and *Arcachon* are suitable in senile cases, and in complications with dry cough and constitutional irritability, where shelter from wind is important.

Ajaccio has much analogy with the Riviera, but is better for patients with great irritability of the system. The same is the case with *Algiers*. on the other hand, cases with much expectoration and with albuminuria generally do better in Egypt and on the Riviera.

The Ocean. — The patients most likely to derive benefit from the sea-voyage are: —

1. Those in whom symptoms of phthisis form only part of a general breakdown from overwork. 2. Cases of limited consolidation without fever. (But it must be borne in mind that the percentage of cures amongst such cases is higher in the Alps.) 3. Quiescent cavity cases often seem to do better at sea than elsewhere; the constitutional and local improvement is most striking.

The contra-indications to a sea-voyage may be enumerated as: —

1. The graver complications, laryngeal and intestinal. 2. Debility. 3. Fever.

It must be remembered that serious illness at sea is a greater misery than on shore. Early hæmoptysis seems not to be aggravated, but cases of hæmoptysis from cavities should on no account be sent to sea, owing to the difficulty of carrying out efficient treatment. The victims of phthisis suffer but little from sea-sickness; the discomforts of sea-life, however, tell so much more on women than on men as practically to exclude the former. Old people, also, the subjects of heart-disease and arterial degeneration, are injuriously affected by the sea.

The treatment of phthisis by climate in the *British Isles* may be regarded in two main divisions: —

1. *The provision* of a summer residence for those who winter abroad.

2. *The choice of a winter resort* for those whose condition or circumstances forbid their going farther afield.

The climate of England, although changeable, is, during the summer, bracing and sedative to the nervous system; in this respect it provides a most useful change to those who have wintered in the more exciting climates of the south. The choice will have to be made between the dry and bracing east coast towns, and the moister, more sedative, and warmer resorts of the south and west. For more vigorous patients, and particularly for those coming from the Riviera, the east coast resorts — Hunstanton, Cromer, Yarmouth, Lowestoft, Felixstowe, Ramsgate and Margate — are suitable during summer. These are often more beneficial to the Riviera patient than the Swiss resorts. The less vigorous, markedly catarrhal, and febrile cases will generally be more benefited by the resorts of the south coast — Bournemouth, Hastings, and Ventnor, or, in the west, Ilfracombe, Torquay, and Falmouth. Ilkley, Malvern, and Tunbridge Wells, again, are excellent resorts for those who are injuriously affected by sea-air. Unfortunately, the English winter climate, owing to its changeableness and number of rainy days, precludes a great deal of that outdoor life so necessary to the well-being of the consumptive. Were the existing opportunities for outdoor life, however, more fully utilised — by sun galleries, etc. — as at Folkestone and still better at Falkenstein, far better results would be obtained.

Dr. Williams' statistics (105) show a slightly smaller proportion of cures from winters at health resorts in England than on the Riviera, and distinctly less than those reported from the Swiss Alps. Although, therefore, the chances of cure are somewhat less than in the foreign resorts, yet the risks are smaller. Early cases, in which the course of the disease requires to be watched before deciding upon the trial of a foreign climate, may have the benefits of one of the home resorts. For cases of early consolidation, without fever, or for partially arrested cases, England is a safe abode all the year round. There remain besides, as Dr. Wilson Fox (31) pointed out, a certain number of patients who, after trying foreign resorts without benefit, improve even in the most unlikely situations in England. But we have no indications to guide us to their recognition. Cases of laryngeal phthisis should seek the milder resorts on the south coast if there be any doubt as to the advisability of their going abroad. More severe and advanced cases will find opportunities for a fair amount of outdoor life without the discomforts of a probably fruitless journey abroad.

The choice of a locality rests between Bournemouth, Ventnor, Torquay, Queenstown and Hastings. Hastings is not adapted for other than the hardier cases; Torquay and Queenstown are relaxing, but well suited to patients with little constitutional vigour. Bournemouth and Ventnor are more suitable for earlier cases in the first and second stages.

In conclusion, it must be borne in mind that though we have some few clinical rules which may help us in the selection of a climate, yet the issue of the selection lies mainly in the patient's own hands. Those

patients do best who bear in mind that climatic change is the smallest factor in the treatment which is to restore them to health, and setting before themselves the recovery of health as their single aim, submit to a regulated manner of life. Nor can we ignore in this respect the sanatorium method of treatment against which such unfortunate prejudice exists, but which has undoubtedly yielded admirable results.

Bronchitis, or **Chronic Bronchial Catarrh,** in young people is in general better influenced by mountain climate than by the sea-side; but in old persons the mountains are often injurious, and amongst the localities abroad the warm sea-side places of the Riviera or the climate of Egypt, of Algeria, of the south-west of France or of the Canaries, are beneficial; or Hastings, Bournemouth, Ventnor, Falmouth, Penzance in England. Whenever there is much expectoration the drier climates are better than the more humid; but if there be irritable cough without expectoration, the latter are preferable, such as Madeira, Algiers, Pau, Arcachon, Torquay, Queenstown. In albuminuria, however slight, the mountain climates are to be avoided, while Egypt and the Riviera are often beneficial; the same is mostly the case with gouty bronchitis.

Emphysema with much expectoration is favourably influenced by dry and warm inland and coast climates; if it be attended with dry cough, the more humid climates of Madeira, Pau, Algiers and Torquay are preferable. High elevations are not suitable, but moderate elevations are so in summer.

Asthma often does not allow a decided opinion without a trial. Of two apparently similar cases one may bear a certain place well, the other not. In general we can say that younger subjects are more benefited by long residence in the Alps than by any other climate or place. If possible their education should be conducted at high elevations. Senile patients with much expectoration ought to try Egypt or the Riviera; with little expectoration and irritating cough, Pau, Arcachon, Algiers, Ajaccio, or South Devon and Cornwall in England, or Queenstown in Ireland. Many asthmatic persons are better in London than elsewhere. In nervous asthma a cautious trial is required to find the most suitable localities.

Scrofula in its various forms requires improvement of nutrition, and mostly acceleration of tissue change. Residence at the sea-side is most useful. Scrofulous children ought to be educated at the sea-side. The sea-coasts of England are pre-eminently adapted to this treatment; but in delicate children, with little reactive power, the winters ought to be spent at warmer coasts, such as the Mediterranean, or Ajaccio, or Algiers, or Biarritz, or Arcachon. Sea-voyages are likewise very useful. Alpine climates, too, offer advantages, but in the majority of cases the sea is to be preferred.

Gouty and **rheumatic affections** are aggravated by damp cold and winds. They require dry soil and warm and dry inland climates, such as the desert of Egypt or Algeria, and southern slopes of mountains, or fairly warm sea-shores.

Affections of the heart include so many varieties that each class of

case requires special management. On the whole high elevation ought to be avoided, excepting in mitral cases with good compensation. Moderate elevations from 500 to 2500 feet with level walks are mostly preferable to the sea-shore. The winter should be spent in warm inland climates.

In **diseases of the kidneys** and **chronic catarrh of the bladder** warm and dry climates act beneficially, by rendering the skin more active, and thus relieving the work of the kidneys. Good milk ought to be obtainable at the resorts for these complaints. Elevated regions are mostly unsuitable.

The **diseases of the organs of digestion** are so multiform that one cannot lay down general rules. In convalescence from chronic catarrh of the colon and dysentery of malarious origin, dry elevated regions are useful. The same is the case with chronic flatulent dyspepsia, which often disappears rapidly on ascending, for instance, from Italy to the Engadine. Dry and warm inland climates may likewise be recommended, especially where high elevations and sea-voyages are not suitable. Localities which offer inducement to open-air exercise deserve special attention. If, as frequently is the case, these complaints are only symptoms of nerve affections, the latter demand the principal consideration.

Malarious affections in general are benefited by high elevations with dry and sunny air, and in summer especially by the air of glaciers.

Cases of **anæmia** and **chlorosis** require climates where the invalids can sit or lie the whole day in the open air without fatigue — such as sunny moderate elevations, and the cooler marine resorts in summer and the warmer in winter. Sea-voyages and yachting are useful for good sailors. Only a moderate amount of exercise is to be permitted, with easy and genial mental and social occupation, and inducement to take a proper amount of food.

In the treatment of **affections of the nervous system,** especially in those called *functional*, climate can take a fair share. In **mental depression,** and also in different forms of **hypochondriasis,** travelling, sea-voyages, frequent change of residence to places of historical interest, which afford at the same time social attractions and facilities for open-air life and exercise, are often attended with excellent results. Rome, Florence, Naples, Sicily, Egypt, Athens and Greece, Palestine and Asia Minor, have in our experience often assisted recovery, and enabled the sufferer to return to home life and active mental occupation.

In **cerebral exhaustion from overwork,** or from ill-regulated and unsuccessful work, and in the numerous forms of nerve failure in men as well as women (Weir Mitchell's *Wear and Tear*), often comprised under the much-abused term of "**neurasthenia,**" change of climate and surroundings is often an essential help; but the nature of the change must depend on the degree of exhaustion and on the mental and physical constitution of the invalid. In cases not too advanced occurring in fairly robust persons, prolonged residence near glaciers, or at all events in the Alps, in winter as well as in summer, with graduated exercise and in cheerful company, has often proved most beneficial; while in cases of greater

exhaustion or of low resisting power, better remedies will be found in yachting in warmer regions; and in wintering in the Riviera, in Algiers, in Sicily, in Rome, in Naples, or in Egypt, where under such circumstances the Nile journeys on a dahabeyah are more restful and mostly preferable to those on steamboats. Time, however, is necessary, varying from some months to some years.

Neuralgia is to be treated according to its nature. If it be of gouty or rheumatic or dyspeptic origin, it falls under these several heads; if, as is often the case, it is one of the earlier symptoms of nervous exhaustion, the suggestions given above are applicable to it.

Diabetes, if acute, requires strict treatment at home; but in persons affected with chronic diabetes, or with different degrees of glycosuria (which are of widely varying nature), climatic treatment can be rendered more or less beneficial according to the nature of the case. In gouty constitutions, for instance, where corpulence is not rare, and where glucose in the urine often alternates with excess of uric acid, the indications are similar to those in gouty and corpulent persons. In invalids, where glycosuria is one of the manifestations of nerve failure, we may recommend, according to the degree of strength and resisting power, long residence at high elevations, or sunny inland and sea-shore localities. In addition to the considerations mentioned under the head of affections of the nervous system, we have in glycosuric cases to bear dietetics in mind, and see that the plan of diet recommended can be carried out.

Polyuria or **diabetes insipidus** is mostly a symptom, sometimes one of the earliest, of disorder of a nerve centre. As valerianate of zinc and similar remedies have a beneficial action, so have Alpine climates combined with open-air life, but without fatigue.

In the state of convalescence from acute disease climatic treatment is often very useful, especially in **tardy convalescence.** We have to bear in mind that the whole system is weakened, and that there is increased liability to disease of different organs from over-fatigue in travelling, injudicious exercise or food, cold winds, damp, etc. It is, therefore, often advisable to begin with change to a good place within easy reach, and to proceed later to more distant localities. Great heat and cold are equally to be avoided, and much patience is often required. Important though this subject be, in a climatic point of view, we must restrict ourselves to these cursory remarks, and leave more detailed suggestions to the authors on the several diseases.

Climacteric changes, in the wider sense of the term, frequently need climatic treatment. The deviations connected with the so-called "change of life" in women are well recognised; but in both sexes the quick rise to a higher stage of development, as well as the rapid descent to a lower stage, and also the delay of development, are often attended by a variety of disorders of the nervous system which manifest themselves in physical and mental disorders of most varied nature. The development and the cessation of the sexual functions are the most perceptible signs of climacteric periods; but other important functions undergo like

changes, and the harmony or equilibrium of the whole organism becomes sometimes disturbed for shorter or longer periods. The more invigorating climates are mostly preferable, but diversion of the mind greatly assists the adaptation of the altered functions to the system at large. We have to bear in mind that there is increased "vulnerability," and that over-exertion and other risks are to be avoided; otherwise the physical climatic elements of places need not be so carefully selected, while localities offering change, exhilaration and mental recreation deserve special recommendation, such as Florence, Rome, the Gulf of Naples, Sicily, Greece, Spain, Asia Minor, Egypt, Algeria, the United States of America, the artistic centres of France, Germany, Holland and Belgium, and so forth, according to the nature of the individual cases.

Senile decay, whether simply natural, or premature, is to be regarded as one of the climacteric changes; but in these cases we have to meet permanently diminished vital powers; hence the necessity of looking for localities where the demands on the weakened organism are more moderate than at home, and the mental faculties are at the same time gently stimulated. The first Lord Brougham showed his wisdom in spending the winters of his advanced life at Cannes.

We could go on almost indefinitely to enumerate morbid conditions which can be benefited by judicious use of climatic changes, but for a mere survey we have probably said enough. We must content ourselves with a mere allusion to the **prophylactic** value of climates. As we have alluded under the head of scrofula to the advisability of educating children with scrofulous tendencies at the sea-side, so we may say that in hereditary or acquired tendency to tubercular phthisis education at well-selected elevated localities is much to be recommended, for instance at St. Moritz, Davos, or "les Avants."

Moreover, we constantly meet with persons who have no measurable disease, but are in a state of health, physical or mental, in which slight injurious influences may do mischief. In such states a judiciously arranged climatic change will often lead to the recovery of health and energy.

Utilisation of Home and Home Climates. — We will restrict ourselves in this chapter to the life of the invalid in English climates and in his own house. We must consider the disadvantages as well as the advantages. We cannot help acknowledging that there is some truth in the description which that sympathetic observer, the elder Dumas, puts into the mouth of D'Artagnan in *Vingt Ans Après*, the "pays où il fait froid toujours, où le beau temps est du brouillard, le brouillard de la pluie, la pluie du déluge; où le soleil resemble à la lune, et la lune à un fromage à la crême." Nor can we forget that we frequently meet with cases similar to that of a singer from Spain whom we often found on her sick-bed humming words from Geibel's "Spanish Gipsy Boy in the North."[1]

[1] She was a consumptive patient who was unable or disinclined to eat, and whom we could only induce to do so by the constant promise to send her to Malaga, where she ultimately recovered.

Dieser Nebel drückt mich nieder
Der die Sonne mir entfernt
Und die alten lust'gen Lieder
Hab' ich alle fast verlernt.

Immer in die Melodien
Schleicht der Eine Klang sich ein;
In die Heimath möcht' ich ziehen,
In das Land voll Sonnenschein!

We must acknowledge that the climates of England are rather moist, that the air is often dull and sunless, that rain falls on comparatively many days, and is distributed over many hours, that the wind is often high and chilling, and that the shelter is limited. On the other hand, the hygienic conditions are better than anywhere else, the food is good, and the separation from the family is less. The climates of England belong, as we have said, to the most health-giving climates for the fairly vigorous, but are less good for the delicate invalid. If, however, a delicate person is obliged to stay at home or near home, it is often possible for him by judicious management to obtain great benefit by availing himself of all the advantages, and defending himself from the injurious influences of the home climates.

It is doubly necessary for him to attend under medical guidance to the seven points which we formulated on page 285. If we carefully examine the good results obtained at foreign climatic health resorts, we often find that they are not so much due to the climatic advantages of those localities as to the hygienic and dietetic management and the whole manner of living. We see, for instance, that the results obtained at Görbersdorf, at Falkenstein, and at Hohenhonnef are at least as good as those gained at Davos, at St. Moritz, and Colorado; and yet in the prominent climatic conditions — namely, the elevation, the number of sunny hours, the diathermancy of the atmosphere — the three former localities are decidedly inferior to the three latter; but in these the hygienic and dietetic arrangements, and especially the open-air treatment and the limits of exercise, are under careful supervision. We could give many instances from which we ought to gain hope that in our home climates, inferior as they are for the management of many delicate persons, satisfactory results may be obtained. A great source of difficulty is that at home the invalid is not inclined to devote the whole day to health matters, to walking or lying in the open air, to taking the necessary numerous meals; but if it be once recognised that life depends on it, the majority of invalids will endeavour to obey.

Most important points for an invalid at home are the selection of a residence and the arrangement of the rooms he lives in. If it be possible for him to choose his house, let it be on a dry soil or rock, on a southern slope, and not at the bottom of a valley; let it be in the neighbourhood of woods, pine woods by preference, and let the woods be between the

prevalent cold winds and the house. An abundant supply of good water is likewise necessary. The house ought to have a sunny verandah with movable glass walls. All the rooms inhabited by the invalid should be towards the sun, and ventilated by day and by night. Couches for lying out of doors or in open verandahs or galleries, and seats with shelter, movable against the wind, ought to be provided. Such arrangements are expensive for single persons; but it ought not to be difficult to found establishments for a number of cases, with diminution of expense and increase of convenience, with well-arranged walks, with large screens against the cold winds; such establishments ought to be under constant medical guidance. There is, we know, a certain amount of prejudice in England against strict medical supervision, but if it were once realised that many lives can be saved in such establishments and under such judicious guidance, which, even at the best climatic health resorts, are otherwise lost, the opinion of the profession and the public would gradually become favourable to them.

It is a matter of great importance that the invalid who remains at his home or in his own country should feel that he is not doomed to die, that he should retain his energy and his firm will to regain his health. Every one of us has many pleasant memories of patients whose cases did not look promising at first, but who, by their firm will and their judicious and dutiful perseverance, entirely recovered under indifferent external circumstances. The qualities of energy, perseverance, and hope cannot be over-estimated in the treatment of chronic disease by climate.

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ARTIFICAL AERO-THERAPEUTICS

By artificial aero-therapeutics we mean the treatment of disease by atmospheres artificially prepared, and differing from the normal either in composition, pressure, or temperature. This will serve as a rough definition of our subject, but it must not be considered as exhaustive, for nature herself supplies exceptions to the normal standard in the varieties of atmosphere caused by the emission of gases in volcanic districts, in the density of air in mines, and in its rarefaction on mountains.

The subject may naturally be divided into two portions —

A. Artificial atmospheres produced by variations in the relative proportions of the gaseous components of air, or those produced by admixture with gases or elements other than those of the atmosphere.

B. Artificial atmospheres produced by variation in the barometric pressure.

Of **artificial atmospheres** we have a familiar example in the air of great cities which contains impurities, varying with the materials used for heating, lighting, and manufactures. In foggy states of the air, such as occasionally prevail in London and other towns, sulphuretted hydrogen and carburetted hydrogen have been detected in the atmosphere; the former arises from sewer gas, and can easily be demonstrated by the blacking of white lead paint on the exterior of buildings; the carburetted hydrogen, the result of the escape of coal gas, may be detected by its odour, unless it have passed through some thickness of earth. In addi-

tion to excess of carbonic dioxide and aqueous vapour, carbonic monoxide, sulphurous acid and ammonia, and organic matter are present; and if there be factories, unless the Smoke Abatement Act be rigidly observed, their products mingle with the atmosphere, making it deviate still more from the normal. Thirty years ago the air of Manchester contained so much sulphurous acid that the late Dr. Angus Smith was in the habit of saying that when it rained in Manchester it did not rain water, but dilute sulphuric acid from the condensation of the sulphurous acid fumes in water.

We must, however, confine ourselves to those modifications of atmosphere which can be applied to the treatment of disease, and we must likewise extend our observations to the application of gases of different kinds to therapeutic uses.

A. Medicated Atmospheres. — *Inhalation* is the most common form of applying medicated atmospheres to the human body, the lungs being the medium of communication. The best instances of inhalation are certain gases, such as oxygen, nitrous oxide and carbonic acid, which have been used for therapeutic purposes; and again the vapour of certain medicines volatile at low temperatures, such as ether, chloroform, nitrite of amyl, tetrachloride of carbon, iodide of ethyl and the like.

There is no method of artificial aero-therapeutics so successful as this; in most cases the full physiological effects of the drug are produced very speedily, as is seen in chloroform inhalation, where a few seconds or minutes suffice to render the patient unconscious: as the gaseous nature of the agent renders it easy of absorption by the lungs, it passes speedily by the circulation to the brain and spinal cord, producing characteristic effects.

The methods of inhalation principally in use are as follows:—

I. Inhalation of gases, such as oxygen and nitrous oxide. II. Inhalation of vapours of certain medicines volatile at low temperatures, such as ether and chloroform. III. Vapours of substances requiring heat for volatilisation, such as mercury and sulphur. IV. Moist warm inhalations. V. Cold medicated sprays.

I. Of the first class the inhalation of *oxygen* has lately come into extensive use to relieve dyspnœa and cyanosis in pneumonia, capillary bronchitis, and like states. It would appear that oxygen combines with the hæmoglobin of the red corpuscles of the blood, and that the quantity absorbed depends upon the pressure of the atmosphere and the amount of hæmoglobin present in the blood. Paul Bert took blood which, under the ordinary atmospheric pressure, absorbed 14 per cent by volume of oxygen, and shook it up with oxygen under increased atmospheric pressure; he found under 6 atmospheres it contained 19·2 per cent by volume of oxygen, under 12 atmospheres 26 per cent, and under 18 atmospheres 31·1 per cent, thus absorbing the element in accordance with Dalton's well-known law of gases. The highest limit of absorption reached in animals inhaling an atmosphere containing oxygen of increased density was 28 to 30 per cent by volume of oxygen in arterial blood.

Pure oxygen under a pressure of 3·5 atmospheres was fatal to animals, inducing first slight trembling of the extremities, followed by stronger convulsions repeated at regular intervals, but becoming weaker and weaker till death supervened. For therapeutic purposes oxygen is supplied under high pressure in iron cylinders; the gas is admitted into an intermediate india-rubber bag whence it flows through a mouthpiece or tube into the mouth, or in some cases through a pipe inserted into the nostrils.

This means has been tried in apparently desperate cases of pneumonia and of capillary bronchitis where cyanosis and unconsciousness have been the striking features. In almost all these patients improvement has followed; the colour has brightened, consciousness has returned, and respiration and pulse rates have fallen; but in many of them the improvement was but temporary, though the rally might be repeated more than once before death, which was usually sudden. Such is my general experience; but in one case it certainly bridged over the crisis, and permanently relieved the dyspnœa and cyanosis. In all the successful cases of oxygen administration in pneumonia the improvement and ultimate recovery seem to have depended on the continuous use of the remedy; it is therefore better to administer oxygen in smaller quantity for hours, possibly for days, than in a large quantity for a short time. It is possible that the sudden deaths recorded may be due to over-stimulation and exhaustion of the respiratory or cardiac centre by the oxygen. This inhalation has been used in the cyanosis of advanced emphysema and in asthma, but only with temporary benefit in either. During their balloon ascents the French aeronauts Croce-Spinelli and Sivel succeeded in alleviating and even dispelling the symptoms of giddiness, nausea, faintness, and the increased respiration and pulse rate by inhaling a mixture of oxygen and nitrogen containing from 40 to 70 per cent of the latter; this they began to use at an elevation of 5000 metres.

Nitrous oxide, or laughing gas, on account of its harmlessness, is largely used as an anæsthetic, especially by dentists. It is also employed during surgical operations, but seldom alone, as its effect is not sufficiently lasting.

Carbonic acid in small quantities has been inhaled for phthisis and other lung affections, and is reported to have a sedative effect on the cough. It is far too dangerous a gas to use as a therapeutic agent,[1] though we often witness its influence on man in atmospheres rendered impure by human exhalations: here, however, the percentage of carbonic acid is still small, and possibly some of the evil effects may be due to other

[1] Carbonic acid, mixed with sulphuretted hydrogen, has been used by Dr. Bergeon of Lyons, as a gaseous injection per rectum. Claude Bernard showed that certain gases, toxic when inhaled, might be absorbed by the colon in large quantities without any bad effects, and thence passing into the portal system, and reaching the heart and pulmonary circulation, be eliminated from the system through the lungs. Dr. Bergeon professed to cure lung tuberculosis in this way, but the treatment failed after a fair trial at the hands of myself and others.

impurities, such as the organic matters mingled with it. The symptoms of excess of carbonic acid in the air are headache, drowsiness, vertigo, and, in time, increasing feebleness of the heart's action with slowness of pulse, the respirations being quickened even to gasping. I have often thought that the relief which suddenly comes to asthmatics at the height of a paroxysm, when lividity and feebleness of pulse proclaim the accumulation of the products of respiration in the blood, may be due to the lowering of the sensibility of the nerve centres by the carbonic acid. I remember a female asthmatic in whom, during a severe spasm, there was complete cyanosis, the nails and lips turning quite blue. The respirations became fearfully laboured, the pulse slow and irregular, and at last apparently stopped altogether. She fell back in the bed, and my assistant thought she was dead; but at the next moment the colour returned to her lips and face, the pulse beat again, she heaved a deep sigh, and her breathing once more became easy. I could not account for these phenomena in any other way than that the accumulation of the gases of respiration, and principally the carbonic acid, acted as an anæsthetic to the medulla and the pulmonary and cardiac plexus.

Chlorine was largely used by the late Dr. A. T. Thomson, who considered it "the best topical expectorant and the most salutary excitant to the mucous membrane that had yet been inhaled"; other authorities, like Laennec and Dr. Stokes, found chlorine too irritating for inhalation. It was at one time largely used for disinfecting purposes, and is very effective, but its strong, pungent smell is offensive. A useful and less pungent form of inhalation is chloride of ammonium vapour: this is made by mixing the vapours of liquid ammonia and fuming hydrochloric acid, the chloride of ammonium fumes are then purified from any excess of hydrochloric acid by passing them through water. Thence they are drawn through a tube into the pharynx, larynx, and nasal passages, and prove beneficial in pharyngeal and nasal catarrh.

Iodine was employed for inhalation by Laennec, Berton, Murray and Scudamore for the treatment of phthisis; the patients either inhaling the vapour itself for a short period, or being surrounded by an atmosphere strongly impregnated with iodine. All these authors speak very favourably of the results obtained. My personal experience of the iodine vapour is favourable, but I have never seen it arrest tuberculosis. Iodine is a strong antiseptic, and probably exercises a bactericidal action on surfaces immediately exposed to its influence, but that it has any effect on the progress of tuberculisation in the lung itself I much doubt. Iodine vapour has been administered with advantage in laryngeal diseases.

II. In the second method certain liquids are used which are volatile at low temperatures, such as ether, chloroform, bichloride of methylene, tetrachloride of carbon and the like. These are almost entirely employed as anæsthetic inhalations, either in a pure condition or occasionally, as in the case of chloroform, mixed with a certain percentage of air; their uses as anæsthetics, however, will not be considered here.

III. The chief substances requiring heat for volatilisation which are used in aero-therapeutics are *Mercury* and *Sulphur*. In the so-called mercurial and sulphur baths the patient, covered up with a sheet, sits on a chair, with a spirit-lamp or gas-jet underneath by which the drug is heated to vaporisation; the vapour envelops the patient, and is absorbed to a large extent by the skin. If the evaporation of steam accompany this process the skin is better prepared for the reception of the drug. From time immemorial, mercurial vapour has been used in India and Arabia for exciting salivation in certain diseases, and it was employed later in the south of Europe. In England the practice was resuscitated by Jackson, and more completely by Mr. Henry Lee, who introduced mercurial baths largely into the treatment of syphilis. Mr. Lee used calomel, and, in order to get rid of the possible excess of hydrochloric acid, baked the calomel before each bath: in this method the powder is laid on a circular plate, surrounded by a trough containing water which the flame soon converts into steam; at the same time the calomel is vaporised. The patient is enveloped in a cloak which, fastened round the neck, prevents the calomel vapour from escaping; this is occasionally unfastened during the fumigation to allow of a short period of inhalation also. Another method of mercurial fumigation is by Trousseau's cigarettes, which consist of blotting-paper soaked in a solution of nitrate of mercury and nitric acid. These were recommended by Trousseau for chronic laryngitis, as well as for syphilitic pharyngitis and laryngitis. The sulphur baths are prepared and conducted in the same way as the mercurial; and have been employed for scabies and other parasitic affections of the skin.

IV. For moist, warm inhalations, where *steam or warm water vapour* is the medium for applying medicinal agents to the lungs, the apparatus vary greatly. The simplest form is a wide-mouthed jug or gallipot filled with boiling water into which a drug is thrown; the patient, taking deep respirations, draws the vapour into his mouth and nostrils through a napkin arranged in the form of a tube. More complicated are the steam spray apparatus of Siegle, Oertel, Robert Lee, Codman and Shurtleff, and others. In some hospitals, as in the Brompton, steam and sprays are fitted up in separate rooms, so that the patients can inhale without admission of the moist air into the ward. This class of inhalations beneficially affects the bronchial tubes, specially in inflammatory or catarrhal conditions, by promoting secretion; but it is doubtful whether they penetrate deeply, or go beyond the primary and secondary bronchi. *Steam sprays* saturate the atmosphere with moisture, which is not always desirable in lung diseases; moreover, they cause excessive skin perspiration. The spray, whether it be a steam or handball apparatus, is produced by a strong transverse current passing over a perpendicular tube; as the air in the upper part of that tube is thus rarefied, any liquid in which the tube may be immersed ascends, and, as it meets the current, is broken into spray. Boyle's well-known ventilating extractors act in the same manner. The apparatus introduced by Sales-Giron, Matthieu and Bergson consisted of two pointed tubes at right

angles, placed with their extremities together, and so joined that the extremity of the perpendicular tube should stand in front of the axis of the horizontal tube. As the stream of air or steam passes along the horizontal tube the medicated fluid rises in the vertical tube, and, on meeting the air current, is broken into fine spray.

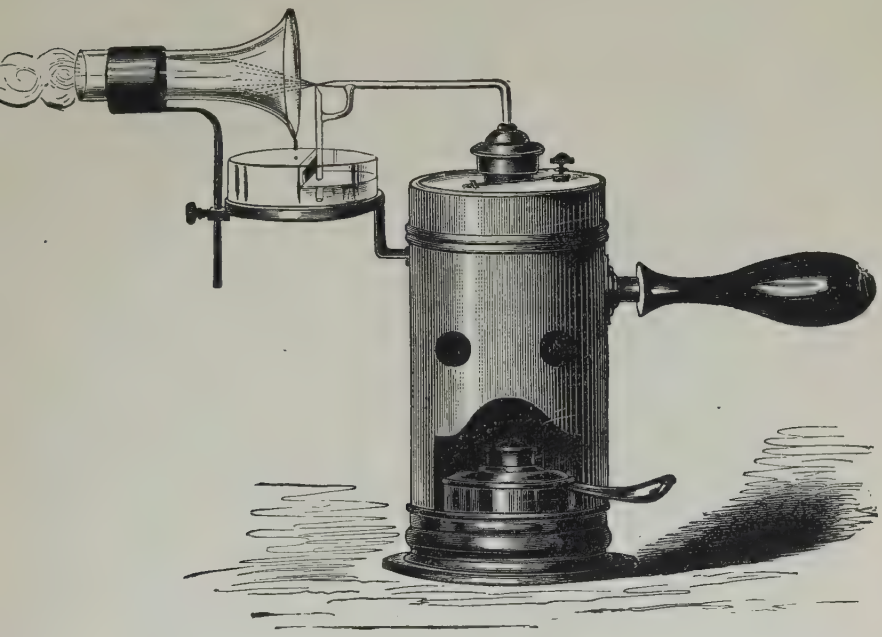

FIG. 15. — Oertel's Steam Nebuliser.

The method is the same, whether air be used, as in the well-known handball spray apparatus, or steam, as in Siegle or Oertel's "steam nebulisers."

The *handball sprays* are used at ordinary temperatures, and as a rule are not so grateful to the patient as warm vapours. They are very useful for the medication of the mouth, the pharynx, and even the larynx; and solutions of quinine, chlorine, or carbolic acid can be well applied through them. They seldom penetrate beyond the larynx and larger bronchi, and generally condense into liquid on the fauces and pharynx. The sprays of mineral water in use at Aix les Bains, Pirrefonds, Mont Dore, Cauterets, etc., belong to this category, and are of use in laryngeal and bronchial affections, but seldom in lung diseases. The free application of antiseptic sprays for purifying the atmosphere of sick chambers and of hospital wards is excellent — carbolic acid (1 in 50), thymol, eucalyptol, or chlorine being adapted to the purpose.

Artificial atmospheres for invalids may be made by *respirators* which

cover the mouth, or, still better, the nose and mouth. These generally consist of metal or celluloid, with two layers of wire gauze or perforated iron plates containing between them cotton wool, tow or sponge on which are sprinkled a few drops of carbolic acid, creosote, terebene, eucalyptol, or other disinfectant. Thus the patient with each respiration breathes an impregnated air, and may do so for any length of time desired. The advantages of these respirators are — 1st, that they admit of the use of certain drugs for long periods; 2nd, that in cases of foul breath, as in bronchiectasis and abscess of the lung, the wearing of an antiseptic respirator purifies the patient's exhalations, to the advantage of his friends and attendants. The patterns are very numerous, such as Roberts', Coghill's, Curschmann's, Hunter Mackenzie's, and Wordsworth's. The most comfortable is Curschmann's: it consists of half a globe of metal, enclosing the mouth, nose, and a portion of the face, from which a short tubes passes for the admission of air. This contains the antiseptic sprinkled on wool or tow between two folds of wire gauze; a strap behind holds the instrument on, and any uncomfortable pressure of the metal against the face is prevented by a layer of air cushion next the skin. The great objection to all respirators is that they interfere with free respiratory movement.

On the efficacy of inhalations as a method of artificial aero-therapeutics, some experiments made by myself in 1888 throw great doubt; these show that inhalations of iodine, supplied by steam or handball sprays, even when given for a considerable period, produce no trace of iodine in the urine; whereas iodine can be detected in the urine after a few doses by the mouth. Turpentine inhalations, on the other hand, produced the characteristic odour in the urine, but not to so marked a degree as when the medicine was administered by the mouth.

The late Dr. Hassall, from careful experiments, came to the conclusion that the greater part of the substances inhaled remained in the inhaler; and that, in the case of the ordinary ori-nasal respirators, four-fifths of the carbolic acid, creosote and other drugs were recoverable from them after the inhalations.

B. Artificial Atmospheres varying in Barometric Pressure must now be considered as therapeutic agents — atmospheres, that is, denser or more rarefied than at sea-level.

The average barometric pressure at sea-level is 29 to 30 inches, at Davos (5200 feet) it is 25 inches; on the summit of Pike's Peak, Colorado (14,147 feet), it is 17·54 inches; and during the famous balloon ascent of Glaisher and Coxwell, at a height of 29,000 feet, a pressure of $9\frac{3}{4}$ inches was registered; indeed, so low a pressure as 7 inches was seen afterwards by Coxwell, though he could not record it. On the other hand, the air is far denser in the deepest mines than at sea-level; and it has been calculated that if a shaft could be sunk forty-five miles into the earth, the air at the bottom of it would be as dense as quicksilver.

Junod was one of the first to apply air at *diminished barometric*

pressure to the human body: in 1835 he contrived a hollow copper ball, $1\frac{1}{3}$ metre in diameter, capable of containing an adult man, and by an exhausting apparatus he reduced the barometric pressure one-third, producing distension of the membrana tympani, dyspnœa, chiefly in the form of short, quick respirations; turgescence of the superficial vessels of the body, as seen in the eyelids and lips; and diminution of the salivary, renal, and other glandular secretions. Junod did not continue his experiments on the general influence of rarefied air on the human body, but turned his attention to the local effects, which were also being studied by Neil Arnott, Murray, and Clanny, and invented the Junod boot and the cupping-glasses, which are still in use. The Junod boot and Sir James Murray's instrument are apparatus for enclosing a limb, or a part of a limb, in an air-tight vessel, and exhausting the atmosphere by an air-pump; the atmospheric pressure being thus removed from the surface of the limb, blood is drawn to the part, the vessels become gorged, and blood is derived from the internal organs. The action of cupping-glasses is, of course, the same in principle.

Dry cupping is useful in congestion of certain internal organs, such as the lungs, kidneys or brain. From the ease and readiness of its application it is of value in cases where blood is to be drawn rapidly from an organ, and especially

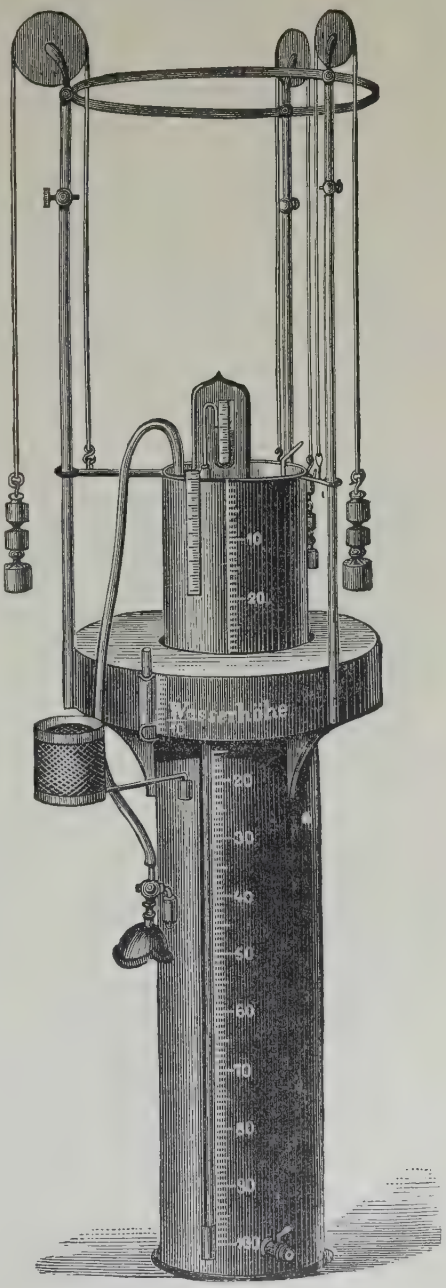

Fig. 16. — Waldenburg's Apparatus.

in hæmoptysis. I have witnessed some of the most profuse hæmorrhages from the lung suddenly brought to a termination by the use of dry cupping to the chest-wall; and I have often observed that so long as the cupping-glasses are kept on the hæmorrhage has been controlled, and that on their removal it may return. Hence the great advantage of cupping-glasses with exhausters attached by which a partial vacuum can be maintained.

This treatment, if carefully applied, leaves no mark, and it is to be preferred to blistering or strong poulticing in cases of gouty disposition or where the patient has a very irritable skin.

The Artificial Application of Air at a Varying Pressure to the Lungs is carried out by various apparatus, most of which are constructed both for rarefaction and for condensation.

It is possible to apply air to the lungs in four different ways:— 1. Inspiration of rarefied air. 2. Expiration into rarefied air. 3. Inspiration of compressed air. 4. Expiration into compressed air.

Of these varieties the only ones found generally useful are the second and third; though in the pneumatic cabinet, to be presently described, the other changes can also be carried out.

The earliest instrument for condensing and rarefying the air was constructed by Hauke, of which Waldenburg's well-known apparatus is a modification (Fig. 16). This last consists of a hollow metal cylinder or bell, containing a certain volume of air, which is plunged into a second and inverted cylinder containing water. By means of pulleys and weights an equilibrium is established, and a pipe is passed from the air cylinder through a drying-box to a mask fitting the patient's mouth; through this he respires the air, which can be rarefied or condensed by raising or lowering the cylinder in the water. This is done in the first instance by drawing off water, in the second by placing weights on the cylinder.

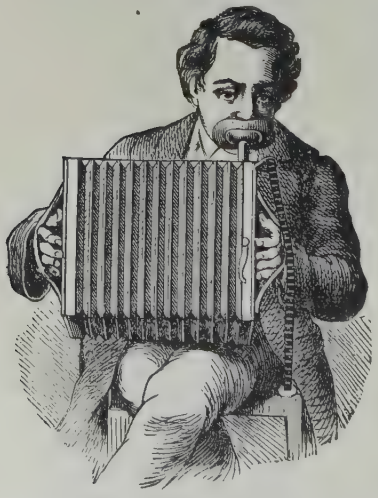

Fig. 17. — Fraenkel's Apparatus.

Some apparatus, like Cube's and Schitzler's second form, are double, and consist of two cylinders, one for condensing and the other for rarefying the air; thus, by changing the tube connections, expiration into a rarefied atmosphere can be followed by the inspiration of condensed air. Others, as Biedert's and Fraenkel's, contain a kind of leathern bellows to compress or rarefy the air as required. Fraenkel's ingenious instrument resembles a concertina with a tube and mouthpiece; it is simple and cheap, and can be worked by the patient himself. The obvious objections to it are

the contracted attitude of the patient, and the impossibility of regulating the pressure.

Lastly, the principle of the centrifugal pump is adopted in Giegel and Mayer's machine, which seems the most complete apparatus of all; in it air, compressed or rarefied by the action of water, is stored up in a central reservoir.

"By the simultaneous use of two apparatuses placed in communication with the mouth of the patient by means of two flexible tubes and a double respiratory valve, and by maintaining the constancy and continuity, a simultaneous rarefaction and condensation of the air can be established, which enables the patient to *inspire* compressed air and to *expire* into rarefied by one and the same expiratory act." For further particulars of this apparatus the reader is referred to Oertel's article on "Respiratory Therapeutics," in the 3rd vol. of *Ziemssen's Handbook of General Therapeutics.*

One of the newest portable instruments for using air at various pressures is the *pneumatic cabinet* of Mr. Ketchum of the United States. A rhomboidal cupboard on wheels, large enough to hold a man in a sitting position, is constructed of steel with a plate-glass window in front; at the back is an air-tight door, which forms the whole side. Above this cabinet is a bellows, worked by a lever, with one set of valves opening into the cabinet, and a second set communicating with the external air: these valves can be reversed, so that by the bellows the air of the cabinet may be condensed or rarefied at will. An artificial wooden glottis regulates the air-stream into the patient's lungs, passes through an aperture in the glass plate, and is connected by india-rubber tubing with the patient's mouth. The pressure within the cabinet is increased by working the lever, or decreased by turning a tap communicating with the external air. In this machine a pressure of two inches can be obtained.

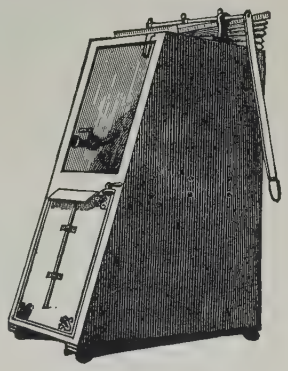

FIG. 18. — The Pneumatic Cabinet.

Various modifications of the respiratory act are possible with this machine. When the artificial glottis is closed, the bellows worked for rarefaction, and the patient makes deep expirations — 1. *Residual air-expansion* results. If he put a nose clip on and adjust his mouth to the glottis tube, which is opened gradually, air from the outside is admitted. 2. *Forced inspiration* results, and a larger volume than usual enters the lungs. The alternation of these two movements, viz., residual air-expansion and forced inspiration, constitutes, 3. *Respiratory differentiation*, an exercise for the purpose of expanding the lungs. 4. *Forced expiration* takes place when the air of the cabinet is condensed, and the patient, having taken a deep breath, expires through the artificial glottis.

The pneumatic cabinet is used for lung gymnastics of different kinds.

A committee of the Brompton Hospital, appointed to investigate its capabilities, showed that its use caused (*a*) increase of chest circumference, (*b*) increase of spirometric capacity, and (*c*), in many cases of consolidation, diminution in the area of dulness. The cabinet was found less successful as a vehicle for medicinal agents, and the remedial effect of medicated sprays in this machine was not greater than at normal pressures. Great caution is necessary in the selection of appropriate cases, and the cabinet must not be used in cases of vascular weakness or of pyrexia — hæmoptysis has followed its use in the former and increased temperature in the latter class of patients.

Many of the described methods of aero-therapeutics depend for success on the exact adjustment of mouthpieces or masks, which are often exceedingly irksome and induce headache and faintness. Another difficulty in many of the instruments is that of supplying sufficient fresh air at the proper pressure; the consequence is that patients have to inhale rebreathed air. To meet this objection the compressed air bath was invented, in which patients are surrounded with an atmosphere in which they can respire air at any desired degree of pressure for hours at a time, and in some cases, as in the St. Petersburg establishment, for days together. Different forms of the bath have been devised, and the size varies according to the number of occupants. The essential elements appear to be (*a*) an air-tight oval chamber of sufficient strength to resist the variations of atmospheric pressure, and (*b*) an efficient compressing apparatus. The chamber may be constructed of masonry or of iron, but more generally it is of wrought iron $\frac{1}{16}$ inch thick, in an irregular or ovoid form, and, if possible, with a domed roof to resist pressure, the whole being strengthened by girders and ribs of iron. The compressing apparatus generally consists of a steam-engine, but in some places, as in M. Fontaine's establishment at Paris, hydraulic power is used which has the advantage of compressing the air, without materially increasing its temperature, and any smell arising from contact with boilers is also avoided. The advantage of steam is the rapidity with which pressure can be increased and steadily maintained.

The annexed woodcut of the compressed air bath in use at the Brompton Hospital will give some notion of the details of the apparatus. The drawing is supplied by Mr. Blake, the manager of Messrs. Haden & Sons of Trowbridge, the constructors of the bath.

The bath consists of three parts: the engine (A), the receiver (B), and the air-chamber (C). A includes a steam-engine D, which, by means of a flywheel and crank, works a second engine E in another and separate compartment F. E is the air-compressing engine, with a cylinder containing an inlet hole and an outlet hole, and in this cylinder works the piston H, the plate of which is perforated by diaphragm valves, not here shown, which close during the descent of the piston and open during its ascent. The air from outside enters the compartment F through the inlet G, and follows the course indicated by the arrows. Entering the air-cylinder it is driven forward by the piston through the

pipe I into the receiver B, containing layers of cotton wool W, into the air-chamber. Both I and J contain valves to prevent a return current.

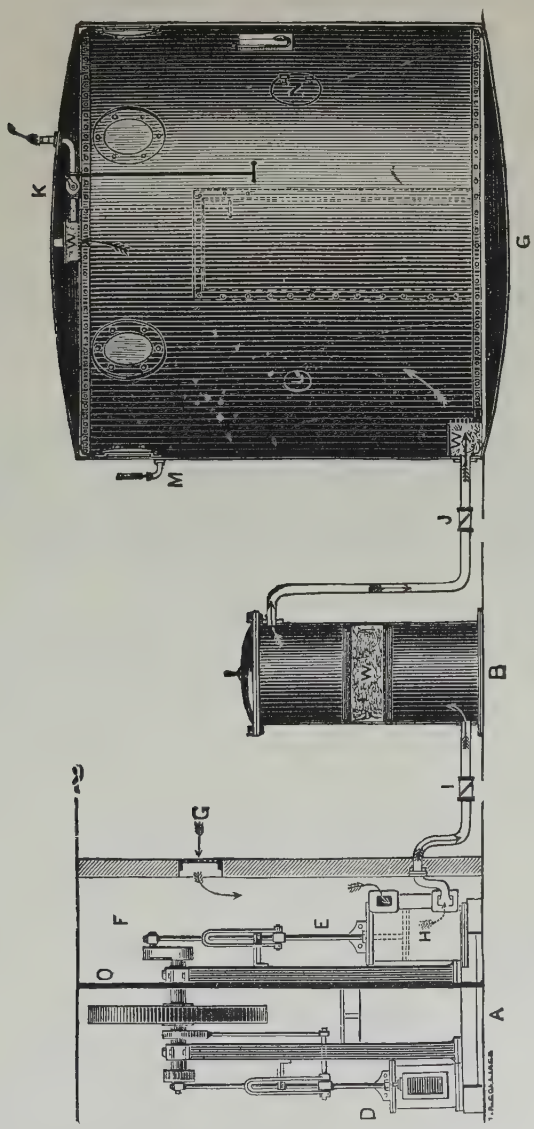

FIG. 19.—Compressed air bath.

The air leaves the bath by an outlet pipe in the roof, which is always open, the strength of the current through it depending on the rate at which the engine works. M is a safety valve which opens wide and blows

a whistle when the full pressure of 10 lbs. is reached. L is a glass spy-hole through which the inmates can be watched. N is an air-tight cupboard, fitted with double bolts to adjust the pressure, by which food and messages, and, if necessary, medicines, may be passed in. Apparatus to regulate the escape of air (K), which can be worked both from within or outside the bath, complete the chamber, which is lit from without by stout plate-glass windows, and fitted with a strong iron door. The air can be changed about five times in two hours, and must be supplied from a pure source, such as a garden or open space, away from machinery and drainage; and in cities it must be filtered through cotton wool in the receiver B. The air rises in temperature during compression, and in summer it is often necessary, for cooling purposes, to pass it over ice before it enters the bath. The extra pressure used for medical purposes varies from $\frac{1}{2}$ to $1\frac{1}{2}$ atmospheres, pressures very different from those which produce the well-known caisson disease, and amount to more than 4 atmospheres. For most diseases, and certainly for lung affections, the added pressure does not exceed 10 lbs. ($\frac{2}{3}$ of an atmosphere); and 9 lbs. above the mean atmospheric pressure is usually sufficient for aero-therapeutic purposes.

The bath or sitting lasts two hours; half an hour is spent in increasing pressure, which is maintained for one hour at the maximum, and half an hour in reducing pressure to the normal. In some obstinate cases of asthma it might be well to maintain the pressure for long periods, and thus enable the patient to live in a compressed air atmosphere for days together. This would be quite possible by means of the air-tight cupboard, through which supplies could be passed. The rate of increase or decrease of pressure should be about 1 lb. in three minutes.

As during compression there is increase of temperature, so during reduction there is a slight fall, accompanied by deposition of moisture in the interior of the chamber. In the management of the bath the chief points to be borne in mind are four: — 1. To increase and reduce the pressure as gradually as possible. 2. To keep the temperature below 65° F. 3. While increasing or maintaining the pressure, to provide for the escape of the used-up or contaminated air. The air should be pumped *through* the chamber, not merely into it; and, as the stream is always flowing, accumulation should only be the result of the outlets being somewhat smaller than the inlets. 4. In case of bad symptoms arising from increase or decrease of pressure, to reverse the process at once.

A healthy person taking a compressed air bath first experiences, as the pressure increases, an unpleasant sensation in the throat, referred to the pharynx immediately behind the tonsil; this is relieved by swallowing saliva or drinking water. Pain is also felt in the membrana tympani, which is due to the different calibres of the external auditory meatus and the Eustachian tube. The latter being much smaller than the former, the column of air, during increase of pressure, penetrates with difficulty to the internal surface of the membrana tympani, and changes of pressure are

slowly communicated; whereas through the meatus air passes freely, and causes under these circumstances a convexity inwards of the auditory membrane. The opposite change takes place when pressure is diminished. Hence the pain and discomfort in the membrane are at the beginning and end of the bath. The voice becomes shriller, and I have known singers gain a note or two above their average while in the bath. The arch of the abdominal wall is flattened, which has been ascribed by Panum to compression of the intestinal gas.

Experiments made by myself and others in healthy individuals show the following results from compressed air: —

Respiration. — The patient breathes slower, deeper and with greater ease. The respiration rate falls from 16 or 15 to 14 or 12 a minute. Von Vivenot records its falling to 5 or even 4 a minute. Inspiration becomes easy, but expiration less so, and the relation between the two becomes changed; whereas at normal pressure the ratio between them is as 4 to 3, it becomes in compressed air as 4 to 6 or 4 to 8. Von Vivenot tells of one case where it was as 4 to 11.

Fig. 20.

The annexed diagram from Von Vivenot shows this as well as the depth of the respiration in compressed air (dotted line) compared with that of ordinary breath (unbroken line).

Spirometric observations show a marked augmentation of lung capacity and chest measurements, a slow but considerable increase in circumference. It would appear that breathing compressed air increases lung capacity, probably by opening up alveoli not previously in use; and the amplitude of each respiration makes up for the smaller number.

Circulation. — The influence of compressed air on the circulation is that the pulse becomes slower and reduced in volume; but the arterial pressure is raised, the superficial capillaries are smaller, and the veins less full of blood. Von Vivenot's white rabbit, when placed in the compressed air bath, admirably exhibited the effect on the circulation. Under normal pressure, the rabbit being quiet and at liberty, the ears were full of blood, the conjunctival vessels injected, and the iris tinted deep red; when pressure was increased, the conjunctival vessels became finer and paler, and in one experiment they visibly filled and emptied.

When pressure was maintained at the maximum, the iris and pupils became discoloured, and the ears, seen by transmitted light, showed empty vessels; even the larger vessels were scarcely visible.

In man the pulse rate diminishes four to twenty beats a minute; but

this depends very much on the temperature of the bath; for, though a prolonged sitting generally causes a fall in the pulse rate, a hot atmosphere will make the pulse rise at first. Sphygmographic tracings show a lowering in the height of the tidal and dicrotic waves, but this change is only maintained during the bath; after it the pulse tracing returns to its former standard. To the finger the pulse appears small and

Fig. 21. — Before bath, ordinary pressure.

Fig. 22. — Pressure, 3 lbs.

Fig. 23. — Pressure, 6 lbs.

Fig. 24. — Pressure, 9 lbs.

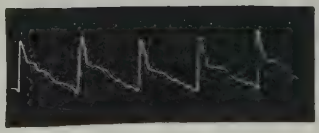

Fig. 25. — After bath, ordinary pressure.

hard. All observations indicate that compressed air exercises an intropulsive influence, affecting naturally the surfaces most exposed to it, such as the skin and lungs, and drives the blood into the organs protected from air pressure, such as the brain, heart, liver, spleen and kidneys. The pressure is exerted more in the capillaries and superficial veins and arteries; and its tendency must be to reduce pressure on the right side of the heart and to increase it on the left. A proof of the fulness of the arterial system is to be found (1) in the sphygmographic tracings, and (2) in the fact that when hæmorrhage occurs in the bath the blood is invariably bright red (arterial). The slower pulse rate, according to Professor Burdon-Sanderson, is the effect of the diminished pressure in the venous system, which retards the filling of the ventricles during the period of relaxation, and consequently lengthens the diastolic period; thus the pulse frequency is diminished.

Again, the introduction of a larger amount of oxygen causes greater absorption of this gas by the lungs, and increased oxidation and tissue change; this is proved by the increase in the amount of carbonic acid exhaled from the lungs, and in that of urea from the kidneys. Appetite is improved and weight is generally gained. Muscular power is stated by Lange to be increased; he found men could carry weights better after the bath than before it.

The internal temperature of the body is slightly raised, sometimes

half a degree in the mouth, that in the axilla being diminished; the rectum temperature (Stembo) rises, as might be expected, from the intropulsive action of the bath on circulation.

From the preceding observations it will be understood that, on account of this intropulsive action on the circulation, the use of the compressed air bath is contra-indicated in congestion, or inflammation, or hæmorrhage of any of the organs which are wholly or partially protected from air pressure by bony cavities, such as the brain, spinal cord, heart, liver, spleen, kidneys, uterus and ovaries. Again fever, in which there is congestion of internal organs, is increased by it.

The intropulsive action is sometimes serviceable, as, for example, in long-standing *amenorrhœa;* for by its effect on the ovaries the bath will often restore the menstrual flow. *Anæmia*, too, is greatly relieved by compressed air baths, probably on account of the large amount of oxygen supplied. Certain it is that under their use pallor gives way to the blush of health, anæmic murmurs disappear, and the number of red corpuscles, as noted by the hæmocytometer, largely increases. This has been my experience in all the cases of anæmia I have treated in this way.

The diseases in which compressed air baths have been found to do most good are bronchial asthma, chronic bronchitis, and emphysema.

Emphysema. — In the tense or large-lunged form, which accompanies bronchitis and asthma, and has been so well described by Dr. C. J. B. Williams and Sir William Jenner, a course of these baths effects a wonderful change. The patient finds he can breathe more freely, and can ascend steps and hills with greater ease. His cough and expectoration are reduced. His respirations are slower and deeper, and the pulse is slower and firmer. Physical examination shows the thoracic distension to be diminished. The line of hepatic dulness, long absent, reappears and rises to the old level, the area of cardiac dulness can again be detected, and the impulse is felt, not in the epigastrium, but in the normal position between the fifth and sixth ribs, slightly to the right of the nipple. Hyper-resonance of the thorax gives place to something more like the normal note; and although there may be prolonged expiration with occasional wheezing sounds, the air is heard to penetrate into blocked portions of the lung in which breath sounds were previously absent. Cyrtometric measurements show a reduction in the chest circumference at different levels of from $\frac{1}{2}$ to $1\frac{1}{2}$ inches; and the spirometric observations yield evidence of "increased vital capacity."

These changes appear to be due to the removal of some of the causes of the emphysema, such as bronchial catarrh and bronchial spasm, thus allowing the escape of some of the distending air from portions of the lung in which the emphysema was perhaps temporary.

Bronchial Catarrh and Bronchitis. — The effect on this class of diseases is excellent; cough is diminished, expectoration first becomes easier and then lessened in amount, breathing is freer, and any accompanying emphysema is reduced considerably. I have used the compressed air

bath in a large number of cases of bronchitis and emphysema, and in every case there has been relief, though it has not always proved permanent. Oertel considers the improvement to be due to the increased pressure on the larger tubes, causing diminution of the blood in the bronchial system, and consequently less exudation of serum into the coats of the bronchi, and less pressure on the lymphatic system.

Bronchial Asthma. — The principal effect of the treatment on asthma seems to be sedative to the pulmonary plexuses and to the pneumogastric nerves. The attacks are rendered less severe, and after a course of twenty or thirty baths the intervals between the attacks become much longer and the spasms finally cease. I have several times placed a patient in the bath during an asthmatic attack, and always with relief to the spasms. In addition to the soothing influence on the nerve-storm, the baths reduce the accompanying emphysema, and more so than in the emphysema of bronchitis, probably because the bronchial obstructions are of a more transitory character. The patient is able to breathe more freely and to take deeper inspirations, the chest distension, as shown by the measurements, diminishes, and the spirometric records increase in amount. Thus an improvement in their general condition ensues. Exercise can be more freely taken, digestion and assimilation are carried on with greater ease and comfort, and strength and colour are gained.

Phthisis. — I have tried the treatment in a large number of cases of phthisis, generally those of limited lung tuberculosis; and beyond the facts that cough and expectoration slightly diminish, and that some portions of the lung become more expanded, I could see no good result. In several of the cases hæmoptysis came on either in the bath or after the treatment, and this constitutes a fresh danger. In some of the patients there was improvement of appetite and gain of weight, but it cannot be said that any lasting benefit resulted.

I tried the treatment in cases of chronic pneumonia and chronic lung infiltration, and also in commencing pleuritic effusion — in the latter case, with the view of inflating the lungs and thus opposing the increasing fluid pressure; but in none of these instances did the bath do any good, and the progress of the disease was unchecked.

The number of compressed air baths sufficient to produce a therapeutic effect varies greatly, but in asthma or bronchitis about thirty are necessary; in chronic emphysema a larger number, sixty to seventy, are often required.

It is a remarkable fact that, while there are numerous establishments for compressed air baths on the Continent and elsewhere, in England there are scarcely any: those best known are the one at Ben Rhydding in Yorkshire, and the admirable one of the Brompton Hospital, which is largely used, and is now made available for private patients.

Respiratory Gymnastics. — Dr. Marcet (8) dwells with great force on the advantage of training the respiration, not only for physiological

exercise, but as an important aid in the treatment of such diseases as asthma. He showed that after forced breathing more than double the weight could be lifted than after ordinary breathing; and he instances the well-known fact of the asthmatic spasm being sometimes momentarily suspended by a forced inspiration, as a proof that a deficient supply of oxygen to the respiratory centres bears a definite relation to the causation of asthma.

Dr. Marcet advocates, as a method of therapeutics for asthma, the practice of the respiratory movements required to carry the air through the lungs in order to oxidise the blood and exhaust the carbonic acid; this practice, at the same time, brings the circulation into better co-operation with the respiratory function. A good form of exercise, according to this author, is "cycling, which increases the depth of breathing, and this without fatigue, the inspiratory movements being automatic; at the same time, it accustoms the rider instinctively to take in at each respiration the volume of air required to aerate the blood, and to eliminate a certain proportion of carbonic acid, leaving in the circulation that amount which is compatible with health."

C. Theodore Williams.

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BALNEOLOGY AND HYDROTHERAPEUTICS

A. — Balneo-Therapeutics; or, Treatment by the Internal and External Use of Mineral Waters

Definition. — The name *Mineral Waters* is applied to those waters which are used in the treatment of disease, either internally or in the form of baths, on account of the saline or gaseous substances which they contain, or on account of their elevated temperature.

The science of the origin of these waters, and of the causes to which they owe their chemical composition and their temperature, is usually called *Balneology*, or in a wider sense *Hydrology;* and may be regarded as a part of Geology and Physical Geography: the art of using them in the treatment of disease is *Balneotherapy*, and mineral waters are a part of Materia Medica.

Our article is not intended as a regular treatise on Balneotherapy, but only as a survey of the uses of mineral waters in the treatment of disease. The external applications of mineral waters in the form of baths and douches, as practised at most of the spas, are, with few exceptions, similar in their effects to those of ordinary water at more or less elevated temperatures. We refer, therefore, for their appreciation to section B on *Hydrotherapeutics;* but we may mention here that at some of the spas various earthy matters are added to the water, such as peat earth or moor earth, and are also used in the shape of local baths or cataplasms.

We will divide the present section into two parts: —

1. Description of mineral waters and their effects.
2. Therapeutic employment of mineral waters.

I. Description of Mineral Waters

The principal constituents of mineral waters are: Water, sodium, magnesium, calcium, and iron; combined with hydrochloric, sulphuric, carbonic, and hydrosulphuric acid. Other substances often present are: Arsenic, lithium, potassium, manganese, bromine, iodine, alum, silica, argon, various organic matters, and other substances in minute quantities. The principal gases are: Oxygen, nitrogen, carbonic, and hydrosulphuric acids.

These substances are derived partly from the surface soil, partly from the rocky strata through which the water deposited from the atmosphere has passed. The differences between the different mineral waters are due to the differences in the superficial soil and the rocks through which the water has passed.

The mineral waters may be divided into groups for more easy survey; for instance, according to their temperatures, or their chemical ingredients, or their physiological or their therapeutical effects. Every

classification is more or less imperfect, and an alphabetical arrangement would be the most easy; but this would entail frequent repetition and thus require more space. We therefore attempt a somewhat mixed arrangement, based principally on the chemical constituents of the springs. It will, however, be evident that some springs contain so large an amount of several ingredients that they can claim a place in different groups; and that others are named not after the substance which they contain in the largest amount, but after that which is held to be most potent. Those thermal waters which are almost devoid of solid substances are placed in a separate group. Thus we may form eight groups: —

1. Simple Thermal Waters.
2. Common Salt or Muriated Saline Waters.
3. Alkaline Waters.
4. Sulphated Saline Waters.
5. Iron or Chalybeate Waters.
6. Arsenic Waters.
7. Sulphur Waters.
8. Earthy or Calcareous Waters.[1]

1. Simple Thermal Waters. — (Syn.: Wildbäder, indifferent thermal waters.) The waters of this group have a higher temperature than ordinary springs, varying between 80° F. and 150° F. or more; they are transparent, very soft, almost tasteless, of low specific gravity, very poor in solid and also in gaseous substances; some contain a little more nitrogen than ordinary water; others claim a little more oxygen. It has been stated that the electrical conditions of these waters are peculiar, but, so far as we know, there is no proof of this.

Matlock, in Derbyshire, deserves to be mentioned in this place, although the temperature of its waters is only 68° F. It lies in a beautiful valley, but the climate of Matlock itself cannot be called bracing.

Many other slightly mineralised warm waters, whose principal action is to be attributed to the temperature of the water, might be mentioned under this head, such as Acqui in Italy and the hot sulphur waters of the Pyrenees; while some of the spas mentioned in the preceding table, such as Leuk, Bormio, Bagnères de Bigorre, Badenweiler, Bath, and Aix-les-Bains, may claim a place in other groups.

The very hot Algerian baths near Biskra, the "Fontaine chaud," (Hammam Salahin, Bath of the Saints) of a temperature of about 112° F.; Mammam Meskoutin, with waters of 170° F.; Hammam R'Irha, 158° F.; and others, may be regarded as belonging to this group.

The United States of America are rich in simple thermal springs which are partly in use, partly in course of development. Some of the most important are — the "Hot Springs" in Virginia, the "Hot Springs" in Arkansas, the "Calistoga Hot Springs," the "Geysers," the "Pass Robles Hot Springs" in California, the "Idaho Hot Springs" in Colorado, the "Warm Springs" in North Carolina, the "Warm Springs" in Georgia, the "Lebanon Springs" in Columbia County, the

[1] For all English Spas, see *The Climates and Baths of Great Britain*, by the Committee of the Roy. Med. and Chir. Society. London, Macmillan, 1895.

"Warm Springs" and the "Healing Springs" in Bath County. We refer for the mineral waters of the United States to Dr. Walton's work (New York, 1883).

Here we ought to mention the large cave of Monsummano in Italy, in which hot vapour is disengaged from numerous surfaces of hot water. The patient walks about in it as in a spacious steam-bath. The benefit derived by Garibaldi has brought new fame to Monsummano. Smaller, partly artificial excavations in the rocks of Battaglia, in the Euganean Hills of Upper Italy, are used in a similar way.

Enumeration. — We can mention some of the best-known waters of this group in the form of a table showing at a glance the two most important points, viz., the elevation above sea-level and the temperature of the springs.

Name of Spa.	Country.	Approximative elevation above Sea in feet.	Temperature of Springs in Fahrenheit.
Panticosa	Spain (Pyrenees)	5000	77° to 92°
Leuk (Löèche-les-Bains)	Switzerland	4600	102° to 122°
Bormio	Italy	4300	90° to 104°
Wildbad Gastein	Eastern Alps	3300	95° to 104·8°
Pfæffers	Switzerland	2115	100°
Johannisbad	Bohemia	2000	86°
Bagnères de Bigorre	French Pyrenees.	1850	90° to 95°
Ragatz	Switzerland	1700	96° to 98°
Badenweiler	Baden	1425	86° to 90·5°
Landeck	Prussian Silesia	1400	66° to 84·2°
Wildbad	Wurtemberg	1323	95° to 98·6°
Plombières	France	1300	65° to 156°
Luxeuil	France	1300	65° to 163°
Neuhaus	Styria	1200	95°
Liebenzell	Wurtemberg	1113	72° to 82°
Warmbrunn	Prussian Silesia	1100	97° to 104°
Tobelbad	Styria	1090	77° to 82°
Aix-les-Bains	Savoy	1060	86° to 120°
Buxton	England	1000	82°
Schlangenbad	Nassau	900	81·5° to 86°
Römerbad and Tuffer	Styria	700–800	81·5° to 86°
Néris	France	800	114° to 125°
Teplitz	Bohemia	650	95° to 120°
Lucca	Italy	500	100° to 120°
Dax	France	130	88° to 140°
Bath	England	100	100° to 120°

Action. — The water of such springs, when taken internally, acts probably like any other pure, not hard, ordinary warm water of the same temperature. We may refer for this use to the article on "Hydrotherapeutics," restricting ourselves to the remark that warm water is more rapidly absorbed by the stomach, and makes less demand on the body by saving the expenditure of heat. We are occasionally told by some patients, whose words are in our note-books, that a single tumblerful of the water of Gastein, or Wildbad, or Buxton, or Teplitz, or Bath, has given rise to striking symptoms, such as the most severe headache, giddiness, inability

to walk, sleeplessness, etc., and, on the other side, to rapid removal of long-standing neuralgia, headache, sleeplessness, mental depression, anorexia, optic disturbances, etc. It is not impossible that these extraordinary effects, good as well as bad, which are quite out of proportion to the quality and quantity of the remedial agent, were due to imagination or suggestion.

Uses. — Drinking courses of these waters are useful in irritable conditions of the mucous membranes of the digestive and respiratory organs, in gastralgia and in some forms of gout and rheumatism.

Bathing courses often act beneficially in allaying great sensitiveness and excitability of the nervous system in its various spheres, and are therefore often resorted to in cases of neuralgia, hyperæsthesia, and hysteria. Their reputation in painful cicatrices and rheumatism in the neighbourhood of old injuries is historical. In chronic rheumatism, in sciatica, and allied affections, in some forms of gout and their remnants, these waters often assist and complete the cure, especially, when combined with Swedish gymnastics and massage.

In the choice of the most suitable spa for individual cases the situation and climate of the spa, the elevation above sea-level, the quality of the bathing arrangements, and the accommodation, are to be considered; and not less so the skill of the medical guidance, and of the persons applying massage and Swedish gymnastics.

2. Common Salt or Muriated Saline Waters. — Although common salt forms the principal ingredient of these waters, many of them contain iron, carbonates of sodium, lithium, magnesium, and calcium, and other chlorides; some also sulphates of sodium, magnesia, and lime, others sulphides and sulphuretted hydrogen, and again others traces of bromine and iodine and other substances. In some of these waters the action is no doubt modified by these admixtures, but as the effect of the chloride of sodium seems to predominate, they have been placed in this group. The difference of different springs is great, not only by the amount of common salt and other solid ingredients which they contain, but also by the presence of free carbonic acid in greater or smaller amount in some of them; and further by the temperature, as some are more or less hot, while the majority are cold. In a larger work it would perhaps be advantageous to make several subdivisions according to strength, according to temperature, according to the presence or absence of carbonic acid, and according to that of other solid constituents; but in this survey we will only mention the more important common salt waters, dividing them according to their situation in different countries.

Enumeration. — The number of common salt waters in various countries is very great. England has the most concentrated salt waters or brines at Droitwich, Nantwich, Middlewich, and Ashby-de-la-Zouche. Droitwich, which has satisfactory arrangements and accommodation, is one of the best places for brine-baths. Moderate amounts of salt are contained in the waters of Woodhall, where they are combined with bromine and iodine in small quantities. Harrogate, situated in a bracing

district of Yorkshire, the most flourishing of spas in England for drinking, and to some degree also for bathing courses, has springs of varying strength in common salt, combined with sulphuretted hydrogen and sulphide of sodium. Llandrindrod (Wales) possesses similar springs, rather weaker, but still useful. At Bridge of Allan, in Scotland, situated in a sheltered position, we have a large admixture of chloride of lime and sulphate of lime. Melksham (Wilts) deserves a place as well here as amongst the sulphated waters. At Leamington and Cheltenham the common salt is combined with so great a proportion of sulphates that these springs may be placed in the group of sulphated waters. England has no thermal saline waters.

In Germany and Austro-Hungary we may mention — Kissingen, Homburg, Soden (on Taunus), Nauheim, Rehme-Oeynhausen, Kreuznach, Wiesbaden, Baden-Baden, Reichenhall, Ischl, Hall in the Tyrol, Hall in Wurtemberg, Hall in Austria, Kreuth, Dürkheim, Niederbronn (Alsace), Krankenheil, Salzungen, Cannstatt, Cronthal, Aix-la-Chapelle (with sulphur), to which many others could be added. Germany does not possess any brine-baths so concentrated as Droitwich and Nantwich, but it has the advantage of several waters rich in *carbonic acid*, as Kissingen, Homburg, Soden, Nauheim, and Rehme; and again some with elevated temperatures, as Wiesbaden, Baden-Baden, Aix-la-Chapelle, Nauheim and Rehme.

France is rich in salt springs of elevated temperature and strong to medium mineralisation: Bourbonne (Haute-Marne), Balaruc (Hérult), Bourbon l'Archambault (Allier), Bourbon-Lancy (Saône-et-Loire), Lamotte (Jura); Uriage (Isère), and St. Gervais (Savoie), with sulphur; Chatel-Guyon (Puy-de-Dôme), with iron. Amongst the cold salt springs of France, Salins (Jura) and Brides les Bains deserve to be mentioned.

Switzerland possesses strong salt waters at Bex and Rheinfelden. In Italy one of the most popular salt spas is Monte Cattini in Tuscany; Castro Caro likewise in Tuscany, is comparatively rich in iodine. Ischia and Castellamare were used in ancient times.

Spain has in Caldas-de-Montbuy, in the province of Barcelona, a strong thermal salt water of great local reputation, and a weaker one in Caldas-de-Malavella in the province of Girone, remarkable for the large proportion of chloride of calcium and magnesium.

Caldas de Rainha, in Portugal, in a beautiful situation, is a most useful weak thermal salt spring, impregnated with sulphuretted hydrogen.

North America possesses St. Catherine's Wells, Michigan Congress Spring, Spring Lake Well, Fruit Port Well, Ballston Spa, and the much frequented Saratoga Springs.

Action. — Common salt is an important constituent of all our organs and tissues; it is an essential part of food, and cannot be dispensed with for any length of time. It plays a great part in the nutrition and metabolism of our body. Owing to its easy diffusibility, a large portion of the salt taken in natural waters is absorbed at once in the stomach, while another part passes into the intestines. It stimulates the secreting

apparatus of the stomach and intestines, the peristaltic action of the bowels, and the circulation in the portal vein. It seems to act specially on the mucous membranes, and to render their secretions less viscid. According to Voit it increases the solubility and diffusibility of albumin, and his experiments corroborate those of Bischoff and Kaupp, showing that an increased supply of chloride of sodium causes an increase in the excretion of nitrogen through the urine. As many persons take at their meals a considerable quantity of salt in addition to that contained in the food itself, the extra amount taken in salt waters, say 100 to 300 grains at the outside, may seem unimportant; but if we take into account that this extra, dissolved in water, is taken on an empty stomach during half an hour or an hour, and that the absorption and diffusion is mostly aided by gentle exercise, it cannot be regarded as insignificant.

Carbonic acid in these waters, as in other mineral waters impregnated with it, seems to alleviate irritation of the sensitive nerves of the stomach, and, by stimulating the minute capillaries and the secretion and peristaltic action of the stomach and intestines, to accelerate the passage of the waters from the stomach into the intestines, and to promote action of the bowels.

In the form of *baths* chloride of sodium and the other chlorides act as stimulants on the nerves and blood-vessels of the skin, and this stimulus seems to be transmitted to the nerve centres and thus to influence the function of internal organs. A feeling of warmth is produced by a warm salt bath greater than is due to the actual elevation of temperature. The presence of carbonic acid in the water appears to heighten these effects. Actual absorption of chlorides does not occur, or, at all events, the quantity absorbed is so small that it may be left out of consideration.

Uses. — The common salt waters are much used in sluggish action of the bowels and stagnation in the branches of the portal vein, with the resulting troubles of dyspepsia, of congestion of the pelvic organs and hæmorrhoidal vessels and enlargement of the liver. They deserve in such conditions to be preferred to "bitter waters" (and also to the alkaline sulphated waters) in spare persons where emaciation is to be avoided. They are also useful in catarrh of the stomach and intestines, and also in catarrhs of the respiratory organs, where they render the secretion less viscid and promote expectoration. In chronic bronchitis their beneficial effect is, no doubt, largely due to the indirect action on the right ventricle and to the improvement in the contraction of the whole heart. Their use (especially that of the hot springs) in chronic rheumatism, in sciatica, and some forms of peripheric neuritis, is well known. Some of them have also long standing reputation in scrofula, as Creuznach, Krankenheil, Woodhall, and in the removal of chronic enlargement of the womb and remains of perimetritis. Many judicious gynæcologists maintain the good effects of these spas in uterine fibroids, although this is not generally admitted.

3. Alkaline Waters. — Waters of this class contain carbonate of sodium as a prominent constituent, and, besides, a varying amount of

free carbonic acid; but many of the waters contain chloride of sodium, and others sulphate of soda in so large a proportion that we are obliged to make three subdivisions: — (*a*) *Simple Alkaline Waters;* (*b*) *Muriated Alkaline Waters;* (*c*) *Sulphated Alkaline Waters.*

Enumeration of the principal spas: — (*a*) *Simple Alkaline Waters* are partly hot, partly cold; the *hot* springs are Vichy (France), Neuenahr (Germany), Mont Dore, Chaudes Aigues, and Néris, in France; the three last are feebly mineralised. Mont Dore has an appreciable amount of arsenic, on account of which it will again claim a place in a later class. The *cold* waters are Rohitsch in Styria, Vals (Depart. Ardèche), Obersalzbrunn (Silesia), Le Boulou (Pyrenees), Evian (Savoy), the Helenenquelle at Wildungen, Bilin (Bohemia), and a number of feebly mineralised waters which are used as *table* waters (Apollinaris, Gerolstein, Fachingen, Geilnau, Giesshuebel, Soulzmatt, Wilhelmsquelle, Taunusquelle).

(*b*) *Muriated Alkaline Waters.* — The principal *hot* springs are Ems (Nassau), Royat (Auvergne), with some lithium and arsenic; La Bourboule (Auvergne), with arsenic; Chatel-Guyon (Puy-de-Dôme), Szczawnicza (Galicia). The *cold* springs are Luhatschowitz (Bohemia), Elster (Saxony), Gleichenberg (Styria), Weilbach (Nassau), Toennisstein (Rhine) and the table waters of Roisdorf and Selters. In North America the Congress Springs in California and the St. Louis Spring in Michigan belong to this class. The California Seltzer Springs contain a large amount of carbonate of magnesium.

(*c*) *Sulphated Alkaline Waters.* — The different springs of Carlsbad (Bohemia) are all more or less hot; the weak springs of Bertrich (Rhenish Prussia) are lukewarm (87° F.); Marienbad (Bohemia), Franzensbad (Bohemia), Elster (Saxony), and Tarasp (Switzerland) are cold, as also Rohitsch (Styria) and a weak spring at Fuered (Hungary).

Action. — Like chloride of sodium, so also is carbonate of sodium an important constituent of the human body, and plays a part in its metabolism. Liebig surmised that it acted as vehicle for the carbonic acid from the blood to the lungs. It has a great share in the secretion of saliva, bile, pancreatic juice, and the digestive processes. Introduced into the stomach, carbonate of soda neutralises the acidity of the gastric secretion, and acts as an antacid; it increases the flow of bile and renders it more fluid; it also renders the intestinal mucus less viscid, and acts as a diuretic. In large doses it is apt to cause emaciation; in small doses it rarely has this effect. The combination with common salt in the muriated alkaline waters further counteracts the emaciating and weakening tendency of the pure alkaline waters, besides which some of the action of common salt mentioned under that head is brought about. A greatly modified effect is exercised by the combination with sulphate of soda in the sulphated alkaline waters. The laxative effect of this salt is predominant; it may be due to stimulation of the nerve ends in the mucous membrane, or to increased exosmosis, or both combined. The increased movement in the intestinal walls leads to more rapid flow of blood in the branches of the portal vein and in the liver itself, and

further assists in the fluidifying effects of the alkalies on the bile and intestinal mucus. By easing the portal circulation the contractions of a dilated heart are improved, and chronic pulmonary catarrh is relieved.

Uses. — Alkaline waters are serviceable in certain forms of dyspepsia where there is a tendency to excessive formation of acid in the stomach, and especially in those cases where this tendency is combined with catarrh of the stomach and intestines; but they are injurious in catarrhal conditions of the digestive organs with deficiency of acidity, as often occurs in anæmia, chlorosis, and convalescence from acute disease. The muriated alkaline waters act beneficially in chronic catarrh of the respiratory organs. The sulphated alkaline waters are often very helpful in atonic constipation, with all its injurious effects on the blood, on the circulation of the portal vein, and consequent passive congestion of the liver; also in tendency to gall-stones, and to uric acid gravel; in some forms of gout, and in the glycosuria of gouty and corpulent persons.

4. Sulphated Waters, or Bitter Waters. — We will apply this name to the waters containing as their active constituent the sulphates of magnesium and sodium. Some of them contain sufficient amounts of chloride of sodium to produce an alteration in their effects. The majority of these waters are used at home, not by residence at the spas.

Enumeration. — Franz Joseph, Hunyadi Janos, Æsculap, and other "Hungarian Bitter Waters"; Rubinat (Spain), Birmensdorf (Switzerland), Pullna (Bohemia), Sedlitz (Bohemia), Saidschutz (Bohemia), Montmirail (Dép. Vaucluse), Friedrichshall (Saxe-Meiningen), Mergentheim (Wurtemberg), Melksham (Wilts), these three with a large proportion of chloride of sodium; the Victoria Spa (near Stratford-on-Avon), Purton Spa (Wilts), Cherry Rock (Gloucester), Scarborough (Yorkshire), Leamington and Cheltenham (*vide* Common Salt Waters).

In this class we may mention Brides-les-Bains in Savoy, with hot mixed sulphated saline springs, containing the sulphates of sodium and calcium and chloride of sodium. These are the only waters of this class which are principally taken not at a distance, but at the place itself which is situated in a beautiful valley, south of the Mont Blanc chain.

Action. — In moderate doses these waters stimulate the mucous membrane of the digestive tract, and increase at the same time the peristaltic actions. In larger doses they cause watery motions. Their action is similar to that of the sulphated alkaline waters described in the preceding class.

Uses. — They are used in habitual constipation, with sluggish circulation in the portal vein and its branches, in passive congestion of the liver, and in excessive corpulency. They have the reputation of removing the latter by an accelerating influence on the retrogressive tissue change of proteinaceous substances. Whether this be so or not, no doubt they remove the alimentary substances from the intestines before all the nutrient has been absorbed; they act therefore as abstractors, and, unless an increased amount of food is taken, the weight must decrease. We often hear that bitter waters are quite mild, certain, and easy aperients; this is the rule with many persons, but the exceptions to this

rule are rather frequent. They act injuriously in most cases of chronic peritonitis and of the resulting adhesions, in ulcers of the stomach and intestines, and in cancerous affections of these organs.

We have sometimes heard that it is more simple to prescribe a certain amount of sulphates in substance and administer them dissolved in hot or cold water; but in our trials of this plan we have frequently found that a much larger dose of the salts thus prescribed was required in order to produce the same aperient effect as a dose of mineral water containing a smaller quantity of bitter salts. We have noticed this especially in using the more composite waters such as Friedrichshall, or Franz Joseph, or Hunyadi, or the sulphated alkaline waters of the preceding class: in like manner a larger quantity of the dried natural salts (say of Carlsbad salts) seem to be required than would correspond to the active quantity of the mineral waters at say one of the Carlsbad springs. It is probable that not all the substances contained in the mineral water are contained in the same conditions and combinations in the salts obtained from it; one point is evident, viz., that the free carbonic acid is lost in the salts. The latter defect may often be corrected by taking the salts in one of the natural acidulated table waters, or in "salutaris" or soda water. Possibly, also, the preparation of these so-called "natural salts" is not always accurate, and indeed may be in some much employed salts intentionally modified, so as to furnish transparent crystallised instead of opaque amorphous salts.

5. Iron or Chalybeate Waters. — This term is applied to those springs in which the proportion of iron to the other ingredients is large enough to produce a therapeutic effect. A great many of the mineral waters enumerated in other classes contain iron; but the amount of other constituents is considered to predominate over the iron. The iron is mostly contained in them as a bicarbonate, with free carbonic acid, and the quantity rarely exceeds four-tenths to six-tenths of a grain in sixteen ounces of water. There are some springs with sulphate of iron in rather larger quantity, but they are rarely used therapeutically. We may divide the iron springs into — (*a*) *pure iron waters* containing only a few grains of other substances in sixteen ounces of water; and (*b*) *mixed iron waters* which contain, besides the iron, a larger but still a small amount of other substances, enough to alter somewhat the character without removing the predominant effect of iron. There is, however, no strict line of division between these groups.

Enumeration. — (*a*) *Pure or comparatively pure iron waters.* — Schwalbach (Nassau), Spa (Belgium), Ceresole Reale in Piedmont, Koenigswarth (Bohemia), Orezza (Corsica), Schandau (Saxony), Alexisbad (Harz Mountains), Brückenau (Bavaria), Flitwick (Beds), Tunbridge Wells (Kent), Charbonnières (Rhône, France). (*b*) *Mixed iron waters* contain, in addition to bicarbonate of iron, bicarbonates of sodium, magnesium or calcium, as Arapatak (Transylvania), Griesbach (Baden), Liebenstein (Thüringen), with bicarbonate of lime; St. Moritz (Oberengadin), Santa Catarina (Northern Italy), Pyrmont (Waldeck), Recoaro (Northern Italy), Reinerz

(Silesia), Sternberg (Bohemia), Godesberg (Rhenish Prussia), Bocklet (Bavaria), Imnau (Würtemberg), Cudowa (Silesia), Kohlgrub (Bavarian Tyrol), Cambray Chalybeate (Cheltenham).

Some possess an appreciable amount of sulphate of soda, as Rippoldsau (Baden) and Driburg (Westphalia), the "Stahlquelle" and "Kalte Sprudel" at Franzensbad (Bohemia), Elster (Saxony).

France possesses two thermal iron springs in Rennes-les-Bains (Aude), and Sylvanès (Aveyron).

A strong iron water is that of Muskau (Silesia), which contains both carbonate and sulphate of iron.

The arsenic waters of Roncegno and Levico, in the Austrian part of the Italian Tyrol, contain large proportions of sulphate of iron.

Action. — The points accepted by the majority of medical men as to the effects of iron waters are: — Increased formation of blood globules; improved contractility of the circulating apparatus, including the heart; better oxidation and heat production; improvement in appetite and general nutrition. A small quantity only of iron is absorbed by the stomach, and none by the skin. The baths of the pure iron springs seem to act like ordinary water-baths impregnated with carbonic acid.

Uses. — Iron waters are, in the minds of most people, the best remedy for anæmia; but their use in this respect is perhaps overrated. There are many cases of anæmia which are not improved, but aggravated, not only by pharmaceutical preparations of iron, but also by iron waters. Anæmia and chlorosis are often caused by constipation and poisoning by ptomaines. In these cases pure iron waters are mostly injurious, while some of the common salt waters and sulphated waters, with or without small proportions of iron, are useful. Many other morbid conditions complicated with anæmia — for instance, malarial cachexia and some chronic skin diseases — are likewise rarely cured by pure iron waters, and this reminds one forcibly of the prescriptions of some very successful practitioners who combine good doses of sulphate of soda or sulphate of magnesia with iron whenever they prescribed the latter.

There are, however, some cases of pure anæmia and some complications of neuralgia, sterility, impotency, and general debility complicated with anæmia, which are benefited by iron waters in drinking as well as bathing courses. In some cases of this kind the compound iron and arsenic waters are indicated.

We have mentioned under the head of simple thermal waters that the degree of elevation above sea-level must be regarded as an important point in the effects produced on the invalid. These remarks are applicable to all the different spas, but especially to the chalybeate class. A course of waters, say of a month, at St. Moritz, or Ceresole Reale, or Santa Catarina, between 5000 and 6000 feet above sea-level, has a different effect on the constitution from that of similarly constituted waters at elevations below 1000 feet.

6. Arsenic Waters. — There are no pure arsenic waters, but the waters containing arsenic in appreciable amounts contain also either iron or

saline substances. Arsenic is, however, so powerful a substance that we venture to place these waters together in a small separate group, in order to direct more attention to them. The group will perhaps be enlarged by further discoveries.

The strongest arsenic waters used at present are those of Roncegno and Levico, which possess sulphate of iron combined with arsenic; they are both situated in the Southern Tyrol, not far from Trento. They are both so strong that the doses required are small, and that they are advantageously diluted with warm water, or with one of the acidulous table waters, or with wine, and taken at or after meals in doses of one or two teaspoonfuls, increasing gradually to two tablespoonfuls. It is advisable to commence with small doses, and carefully to watch the effect, as in some persons they occasionally cause digestive derangements, such as diarrhœa; and in others constipation.

There are now fair hotels both at Levico and Roncegno, but the waters are more used away from the spas themselves.

At Val Senistra, in the Lower Engadine, are springs containing arsenic in smaller quantity (one-fifth of the strength of Roncegno and Levico), combined with carbonate of iron and carbonate of soda.

Ceresole Reale, in Piedmont, has, in addition to bicarbonate of iron, small quantities of arsenic; it is situated in a beautiful and bracing locality, and has good accommodation.

Uses. — These arsenical chalybeate waters are applicable to the same ailments as are the pure and mixed iron waters, but specially deserve a trial in chronic skin affections with anæmia, and in lymphatic and glandular diseases, and in malarial cachexia.

La Bourboule, which we have mentioned already amongst the warm muriated alkaline waters, has so appreciable an amount of arsenic that it demands a preference over other muriated alkaline waters in chronic skin diseases, and may also assist in the treatment of chronic phthisis.

Mont Dore, with a smaller amount of arsenic and alkaline substance than La Bourboule, has a much greater reputation in the treatment of asthma. This is probably due in part to its higher elevation, and in part to the very energetic use of inhalations; which, however, require careful management in delicate persons.

7. Sulphur Waters. — They contain either sulphide of sodium, calcium, potassium, or magnesium, or sulphuretted hydrogen in an appreciable and fairly constant proportion.

In some of the springs, as at Aix-les-Bains and Landeck, the quantity of sulphur is so small that they may be placed amongst the simple thermal waters.

In other sulphur waters the amount of chloride of sodium and other solid substances is so large that they find a place in other classes; such, for instance, is the case with Harrogate, Llandrindod, Uriage, Aix-la-Chapelle, Caldas de Rainha, Mehadia, the Columbia Springs, and the Louisville Artesian Well in the U. S. A. Many of these springs are thermal, but some are cold.

Enumeration. — The best thermal sulphur waters are those of the French Pyrenees — Eaux Bonnes, Eaux Chaudes, Cauterets, Barèges, St. Sauveur, Bagnères de Luchon, Le Vernet, Amélie-les-Bains — which all contain the sulphur as sulphide of sodium, and are situated at fair elevations.

Other hot sulphur waters of great reputation are — Baden, Lavey, and Schinznach in Switzerland; Aix-les-Bains and Uriage in France; Aix-la Chapelle and Burtscheid in Germany; Landeck in Silesia; Baden in Austria; Mehadia and Pystjan and others in Hungary; Battaglia and Acqui in Piedmont; Abano in the Euganean Mountains of Northern Italy; Panticosa in the Spanish Pyrenees; Trillo near Madrid; Caldas de Rainha in Portugal; Hélouan in the Arabian desert near Cairo. Amongst the cold springs Harrogate is best known in England, Llandrindod and Builth in Wales, Strathpeffer and Moffat in Scotland, Lisdoonvarna in Ireland; Challes, Enghien, and two springs at Bagnères-de-Bigorre in France; Eilsen, Nenndorf, Weilbach, Meinberg in Germany; Alveneu, Gurnigel, Stachelberg, and Heustrich in Switzerland.

Action. — Sulphuretted hydrogen is absorbed by the skin and by the stomach, and we know that larger quantities are poisonous by depressing the action of the heart, and by decomposing the blood globules. It is, however, difficult to account for the alleged action of such small quantities as are taken up by the system during drinking and bathing courses. They are said to act as cholagogues, but this is not clearly demonstrated by experiments.

Uses. — They are used in chronic rheumatism and gout, but hot baths and hot water drinking are likewise beneficial, and it is not certain that the presence of small quantities of sulphur adds much to the effect of hot water; the same may be said with regard to some chronic skin diseases. Chronic bronchial, laryngeal and pharyngeal catarrh are benefited; and often also hæmorrhoidal conditions. We have occasionally seen good effects in conditions of great irritability of the heart with palpitation. The ancient reputation of their good effects in poisoning with mercury or lead has become doubtful. Much has been written about the action of these waters in syphilis, but we must not forget that the successful physicians at these spas make most energetic use of mercury.

8. Earthy or Calcareous Waters. — Carbonate and sulphate of lime and carbonate of magnesia are the principal constituents.

Enumeration. — Contrexeville, Vittel, Bagnères-de-Bigorre, Pougues, St. Arnaud, Cransac (contains also manganese and alum) in France; Wildungen, Lippspringe and Inselbad, in Germany; Alzola and Fitero, the latter with hot springs, in Spain; Chianciano, with hot springs, in Central Italy; Weissenburg in Switzerland. In North America the best-known earthy springs are — the Butterworth Springs, Eaton Rapid Wells, and Leslie Well in Michigan; the Gettysburg Spring in Pennsylvania, the Sweet Springs in West Virginia, and the Alleghany Springs in Virginia. The table waters, St. Galmier, Couzan and Taunus, may be placed in this class. Many of the waters mentioned in other classes con-

tain much calcareous matter, as Bath, Loèche, Bormio, Lucca and Füred, classed amongst the simple thermal waters; and Baden in Austria, Baden in Switzerland, Schinznach, Battaglia and Abano amongst the sulphur waters.

Action. — Internally taken these waters exercise, through the carbonate of calcium, an antacid and also soothing effect on the mucous membranes, and are at the same time slightly astringent and constipating, especially when they contain much sulphate of lime. In bathing courses their action is nearly the same as that of simple hot water.

Uses. — They are useful in dyspepsia, with irritability of the mucous membrane, acidity, and diarrhœa. Some of these waters possess a great reputation in proclivity to gravel and stone, and to chronic catarrh of the bladder. They are used also in biliary concretions, and in gouty conditions. Their good effects are probably due in a great degree to the circumstance that these waters can be taken in large quantities, and thus exercise a washing-out effect. In cases of actual stone in the bladder, or in the kidney, the use of these waters is of doubtful value; the concretions may be actually increased by fresh deposits around them.

A speciality at some springs, especially at Loèche in Switzerland, is the treatment of chronic eczema, psoriasis, and other chronic skin diseases, by hot baths prolonged over several hours, and this treatment is not rarely successful, at all events for a certain time; but relapses are rather common.

II. Therapeutic Employment of Mineral Waters

There is perhaps no section of medicine about which the ideas of the educated classes, including many members of our own profession, are so vague as about the effects of courses of mineral waters and baths, especially at foreign spas. On the one side we hear very often that the good effects produced by spa treatment abroad are due not to the waters and baths, but only to the concomitant influences, such as change of locality and habits of living; on the other, we hear that the waters alone are the curing agents, and that they have, or ought to have, the same effect when taken at home. Both views are, however, defective, and based on imperfect observation. The error of the former assertion is due to inferences from cases where the aberrations from health are not great, and are caused only by faults of home life, such as indulgence in food, irregular hours, social or business worry, excessive or unsuccessful work, acute or chronic mental shocks, want of exercise, and unhygienic arrangements. It is not quite so easy to show the error of the latter view, but it is equally real with regard to the majority of invalids. It is a great tax on the system to digest compound mineral waters. There are, it is true, strong persons with imperfect portal circulation, dyspepsia, hæmorrhoidal congestion, and inactive liver, who are able to right themselves by good purgative waters; and can take with advantage even courses of Carlsbad or Kissingen waters while continuing their usual diet and their daily work; but the majority of invalids,

especially those with a delicate constitution, or with a weak heart, do not possess the amount of vital force sufficient for the digestion of these waters, if at the same time their brain or their mind is taxed, if they have to go into society, and take long or large meals in close rooms. They often break down utterly if they attempt to do so. Even at country houses many people cannot disengage their minds to such a degree as to be able to bear these waters; and at the spas themselves it often happens that success is entirely spoilt by attention to letters from home, especially about business or family worries.

On the other hand, we have to deal with the opposite error, viz., the belief of many persons that the power of foreign waters is so great that they think they can remove large tumours, fatty or bony, or carcinomatous; that they can unbend contracted limbs; that they can restore the muscles wasted from infantile paralysis, or the functions lost from senile decay. Incredible as this may appear to the educated medical man, such ideas persist in the high places of society. It is, therefore, very desirable that our profession should devote more attention to this important branch of treatment, and should diffuse general knowledge on the subject amongst the public. For this purpose a few lectures ought to be given regularly at our medical schools on balneo-therapeutics, and also on climato-therapeutics, as a part of the course of Materia Medica. We ought not to be deterred from such a course by the great difficulties which beset the subject, to which we can but briefly allude. While in our pharmaceutical remedies we have to deal with more or less fixed and simple substances, most of the mineral waters are compound; and, even if we know to some degree the action of the constituents severally, we often cannot accurately calculate the share which each of these substances plays in combination with the others, or their mutual interaction — points to which we have already alluded in the description of the different classes of mineral waters. We may call to mind something analogous in our ordinary treatment when we prescribe compound aperient pills, or compound sedative draughts. Another point of some uncertainty is that we prescribe the waters according to their most prominent ingredients, but we cannot be perfectly sure that the substances present in small quantities do not play a more important part in the action of the whole water than we generally concede to them.

We must acknowledge that we have, as yet, no scientific basis for balneo-therapeutics. Our position is still entirely empirical, based on the observation and experience of physicians and patients as to the effects of certain waters and cures, either at home or at the spas; but with all the admissions as to our exactness of knowledge, we are obliged to grant that special bathing and drinking cures are most efficacious in many chronic morbid conditions, and cannot be replaced by any other modes of treatment (32).

We will now endeavour to give a short sketch of the main points which are to be considered by the practitioner who is asked about mineral waters and baths. We must begin in every case with the

question, whether balneo-therapeutic treatment offers advantages over the ordinary medical treatment; and then consider whether this treatment ought to be carried out at home or abroad, and whether it is to be preceded or followed by pharmaceutical or other treatment, or combined with it. When the question is decided in favour of balneo-therapeutic treatment, we have to regard not only the name and nature of disease, but have to study all the conditions and habits of the individual before us, pecuniary, physical, and psychical; his constitution in general; his power of reaction; whether the different organs are healthy or not; whether they can take up increased work in order to relieve the diseased part; whether they are able or unable to respond to any unusual demand. Thus we shall learn whether stronger therapeutic action is permitted; whether rougher journeys and accommodation, colder climates and seasons can be borne; or whether gentle treatment is necessary, with easy journeys, warm seasons, mountain climates of moderate elevation, sheltered and sunny habitations, and delicate food.

The chemical constitution of the waters alone is not sufficient for our selection of the place; we must know the accustomed methods of treatment at certain localities, the accommodation, the quality of food and the cooking, the climate, the social elements likely to be found, and above all the qualities of the local physician to be selected for the treatment of the case.

It must be evident from these remarks that the same morbid condition may in different persons require different localities and even different classes of mineral waters; and, further, that diseases of different nature may be benefited at the same spa, by adapting the various bathing procedures, the doses and temperature of water to be drunk to the individual case, and by selecting, when there are different springs at the same place, the most suitable one. Often the treatment must be at first of a tentative nature, requiring the most careful watching by the local physician, and perhaps frequent alterations. In many cases it is impossible to attack the principal complaint, and our efforts must be directed towards improving the general condition, by which means very often the diseased portion of the organism is drawn into the stream of general improvement.

Taking the different points just alluded to into consideration, every one will see how much depends on the *local physician*; and that it is not in the interest of the patient to prescribe the course of treatment, either directly or indirectly: though it is often advisable for the home practitioner to make suggestions based on previous experience.

We will now sketch the applicability of waters to some morbid conditions, but must limit ourselves for want of space to a few states only.

1. Tardy or imperfect convalescence is the condition of many persons inquiring about waters, and the nature of these cases varies considerably. All have this in common, that they are in a state of instability; their balance is easily upset. Any increased demand on their

nerve power, or on their digestive functions, may lead to illness; the nerves and blood-vessels of the skin are weak; and comparatively slight exposure leads to chill and to more or less grave results. In advising we must therefore be careful to warn against fatiguing journeys, irregular or heavy meals, long cold drives, and so forth. The majority do not require spa treatment; when they do, spas not too distant, with gentle treatment and good accommodation, in sheltered positions at medium elevations, are to be recommended; or change of air alone without spa treatment at the beginning. Later, iron waters or common salt waters are often useful. If there be still remains of disease, each such case will require special consideration.

In the exudations of perimetritis, for instance, after miscarriage or confinement, the common salt waters, such as Kreuznach, Kissingen, Woodhall are useful.

If after rheumatic fever the skin remains weak, the joints painful, the heart dilated, with or without some valvular complication, the thermal gaseous saline waters of Nauheim and Rehme are of great value, sometimes assisted by Schott's movements with resistance.

If tendency to diarrhœa be a prominent symptom, Plombières is often useful; if much neuralgia without organic cause, Schlangenbad; if chronic bronchial catarrh, the muriated or muriated alkaline waters of Soden, of Gleichenberg, of La Bourboule, or of Baden-Baden.

2. Abdominal venosity is a prominent feature of many chronic ailments, not only of the abdominal, but also of the circulatory and respiratory organs — of obesity, of drowsiness, of anæmia, of glycosuria, etc. The term used by the old German authors, *Abdominal plethora*, is very significant. It is often the cause of piles, of the enlargement of the liver, of chronic pulmonary catarrh, and so on; and is generally part of a weak organic fibre in the whole system, of the heart and all the blood-vessels, especially of the capillaries and veins, but also of the intestines and of the mucous membranes. Dietetic and hygienic management, the various forms of active and passive exercise, are pre-eminently useful, but these are greatly assisted and must sometimes be preceded by waters: here the alkaline sulphated, the "bitter waters," the common salt waters are most useful, for an account of which we refer to the first part of this contribution.

3. Diseases of the Respiratory Organs. — Climato-therapeutic treatment is, in the majority of cases, more important than waters, but the latter in many conditions may be a great help, and in others deserve the first place.

In chronic catarrh of the bronchial tubes the alkaline and muriatic alkaline waters and the sulphur waters are beneficial; and when it owes its origin to abdominal venosity, the recommendations of the previous section find a place. When the dilatation of the heart is the prominent feature, the waters and baths of Nauheim, assisted by the movements with resistance, are required.

Emphysema comes more or less under the same head. Climatically

the saps of Gleichenberg in Styria and of the Pyrenees are well adapted to these cases, and so is Ems in the earlier or later summer.

Chronic naso-pharyngitis, if it be not connected with adenoid growths, requires likewise alkaline muriated or sulphur waters, or the arsenical waters of Mont Dore with inhalations.

Imperfect resolution of pneumonia needs climatic and careful hygienic management, and sulphur and alkaline muriated waters, but with careful avoidance of exposure to the raw morning air while taking the early draughts.

Asthma depends on various causes, and accordingly requires various modes of treatment by drugs and water and climate, or is not amenable to any. The catarrhal form in fairly robust persons is often greatly relieved by the treatment at Mont Dore.

4. Diseases of the Heart. — We restrict ourselves to a few remarks. Many cases are not suited to long journeys and treatment by waters.

Fatty hearts or weak hearts in fat persons are mostly benefited by diet, combined with active and passive exercise and with sulphated alkaline and bitter waters. For dilated hearts associated with abdominal venosity, see sub-section 2.

In valvular affections with great anæmia iron waters are often useful; but in many cases aperient waters or pharmaceutical preparations, and Swedish gymnastics, must be combined with chalybeate waters.

In weak and moderately dilated hearts graduated exercise (Oertl) is better than baths; but if the dilatation be great, whether with or without valvular disease, the cautious use of the baths of Nauheim, assisted by movements with resistance, must precede the voluntary movement with climbing. In some cases treatment at home on the Nauheim plan must precede the journey abroad; and sometimes we must not be deterred from such measures by seemingly advanced symptoms.

Recent valvular affections resulting from rheumatic fever we have already mentioned in sub-section 1.

5. In **Anæmia** we have to consider whether it is caused — (*a*) by direct loss of blood or albuminous and mucous discharges; (*b*) by constipation and impeded abdominal circulation; (*c*) by inability to take food, sleeplessness, mental shocks and worry, neuralgia, etc.; (*d*) by diseases of the lymphatic glands; or (*e*) by malarious affections and consequent affection of the spleen and liver. The more a case belongs to (*a*) the more likely is the effect of iron to be beneficial; and the physician has to decide whether chalybeate spa treatment offers advantages over pharmaceutical preparations. In the group (*b*) chloride of sodium waters are mostly preferable at first to pure steel waters; and a course of the latter, or of climatic treatment, or of both combined, may in many cases follow with advantage. In (*c*) climatic change alone is often more important than waters. In (*d*) the use of muriated saline and of arsenic waters may be tried; but they often fail, and ought at all events to be followed by long sea-side residence or sea-voyages. In (*e*) the muriated or sulphated saline waters at mountain localities ought to be combined with

iron or arsenic, and followed by long residence at high elevations or occasionally sea-side places.

6. Gravel and Stone. — In the uric acid varieties the alkaline waters are generally prescribed, but great care is necessary not to allow the urine to become too alkaline, since this may lead to deposition of phosphates around a small uric acid stone. A better plan, in general, is to order the sulphated alkaline waters, especially the hot waters of Carlsbad, in the numerous cases where a certain amount of abdominal venosity and sluggish circulation of the liver are among the causes of gravel.

We have already mentioned that it is difficult to explain the great reputation of earthy waters in gravel, and that their effect is probably due to the administration of such waters in large quantities, so as to produce a washing out effect, which probably would be obtained quite as well by the systematic drinking of large amounts of hot water on an empty stomach.

7. Gout occurs in widely-differing constitutions, varies widely in degree, and may or may not be complicated with many other morbid affections. If we have to deal with persons of so-called "full habit" — with portal venosity, sluggish liver, and a urine of rather high specific gravity, loaded with urates and uric acid — the sulphated alkaline or mild bitter waters are indicated, especially Carlsbad, Marienbad, Tarasp, Franzensbad, Elster, Brides-les-Bains. All courses of the stronger waters ought to be followed by a long rest with careful diet in good air before returning to the daily life; and this is pre-eminently the case with the courses just mentioned. If such a long rest be impossible, a less searching course ought to be recommended, such as, according to the nature of the case, Homburg, Kissingen, Harrogate, Leamington, Royat, Contrexeville, La Bourboule, Wiesbaden, Baden-Baden, Aix-la-Chapelle, Uriage, Aix-les-Bains, Bagnères de Luchon. A shorter rest is usually sufficient after these waters. In many delicate persons, especially if time be limited, the simple thermal waters are preferable — Buxton, Bath, Wildbad, Ragatz, Schlangenbad, Teplitz, Gastein. Numerous cases of gout, however, are not suitable for mineral water treatment, and will be found more amenable to pharmaceutical remedies, diet, and climate.

8. Chronic Rheumatism. — In cases associated with exudation round the joints, the hot thermal treatment is very useful; and it must frequently be combined with various forms of massage and Swedish gymnastics. The simple thermal waters, the hot sulphur waters, the muriated saline waters, can be employed with success. Chronic muscular rheumatism is amenable to similar treatment. In cases combined with affection of the heart, especially with dilatation, the tepid gaseous saline waters of Nauheim are preferable, associated with Schott's modification of Ling's system. Many cases are well suited to simple hydrotherapeutic treatment.

9. Diabetes and Glycosuria. — It is not long since some alkaline and sulphated alkaline waters, especially Vichy, Carlsbad, and Neuenahr, were thought to exercise a specific influence on these complaints; but reason

and experience have proved this view to be erroneous. It is quite true that in the milder forms of glycosuria courses of treatment at these spas improve the general health, and greatly diminish or temporarily remove the sugar from the urine. This, however, is due in the first place to the arrangement of diet, in the second to improvement of the digestive organs and functions by the use of the waters, and, thirdly, to the removal of the patients from the worries of life at home. In the frequent cases of chronic glycosuria in fat and gouty persons, sulphated alkaline waters are beneficial, and the more bracing the climate the better.

10. Diseases of the Nervous System. — Spa treatment is, as a rule, not applicable to mental diseases, although milder forms of hypochondriasis and melancholia, if they depend on chronic constipation or abdominal venosity, may be favourably influenced by the waters mentioned under that head. Epilepsy is likewise to be excluded, and also locomotor ataxy, unless they depend on syphilis, which will be presently discussed.

Nerve exhaustion and neurasthenia in their various forms and degree may, according to the nature of the cases, be treated at chalybeate, or thermal muriated saline, or simple tepid spas; but such treatment can only take a small share in the judicious general management, which must be pursued during a long period of time.

Neuralgic affections are often relieved by spa treatment, if they can be referred to gout, to anæmia, or to nerve exhaustion; and the selection of the spa must depend on these considerations.

11. Affections of the Female Sexual Organs are frequently treated at spas, although such treatment is not always required. Chronic congestion of the womb, especially in consequence of confinements and miscarriages, can be greatly benefited by the muriated saline, by the alkaline, and also by the simple and the sulphurous thermal waters. The deposits round the pelvic organs from perimetritis are often removed by the careful use of the muriated saline waters. Many gynæcologists, both in this country and abroad, have great faith in the effect of these waters (especially those of Creuznach) in fibrous tumours of the uterus.

12. Syphilis is regarded by many persons as one of the diseases which can be cured by the use of mineral waters; but all that can be said is that the use of other remedies may be assisted by them. It often happens that the energetic use of hydrargyrum cannot be carried out under the usual circumstances of home life, and that it is facilitated by the methodic employment of hot baths and vapour baths, and the careful management of the manner of living, so as to avoid chills, and other injurious influences. Thus certain spas, like Aix-la-Chapelle, have acquired a great reputation in the treatment of syphilitic affections, especially those of secondary and tertiary phases. In this way many cases of affections of the skin, of the mucous membranes, of the muscles and organs of circulation, of the brain and spinal marrow, epilepsy and locomotor ataxy, on a syphilitic basis, are cured or benefited more or less permanently, or again it may be but transitorily, by treatment at spas; but generally

not by mere spa treatment. This applies as well to acquired as to inherited syphilitic affections. As in home treatment, so also at spas, it is often found that serious affections on a syphilitic basis are no longer amenable to anti-syphilitic treatment, and that the latter does more harm than good. In such cases the means for the improvement of the general health are all that remain to us, and herein climate and spas may take again their humble share according to the nature of the cases.

We might mention a number of other morbid conditions which can be relieved by spa treatment, but for a mere survey the preceding classes of affections are probably sufficient. We can also dispense with suggestions about diet and manner of living, as each individual case ought to be considered in itself by the local physician, whose assistance, as we have already urged, is indispensable.

Seasons for Spa Treatment. — A few words as to the times of the year to be selected are perhaps not out of place. Climate and weather are important agents in spa treatment. Most delicate persons are better in summer than in winter; spa treatment has, therefore, a greater chance of doing good in summer. Extreme heat, however, is to be avoided in most cases, and spas which are very hot in the middle of summer, such as Wiesbaden, Ems, Aix-les-Bains, Vichy, Baden-Baden, Bath, ought therefore, as a rule, not to be visited in July and the beginning of August, but in the earlier and later parts of the summer. On the other hand, spas at high elevations, such as St. Moritz and Tarasp, ought to be recommended only between the middle of June and September. Few resorts are open earlier than May or later than September; but some of the hot springs, as Bath, Aix-la-Chapelle, Wiesbaden, Baden-Baden, Amélie-les-Bains, and Dax, are available during the whole of the year. It must be borne in mind, however, that much greater care is required in the hot baths during the colder months, and that the exhilarating influence of fine weather is mostly wanting.

Duration of Courses of Spa Treatment. — Formerly it was the custom to have fixed periods for the treatment at different spas, say three, four, or five weeks; but in the light of increased knowledge, we have learnt that it is in many instances impossible to fix at the outset the length of the course — just as it is often impossible to say, on prescribing iron or arsenic, that it is to be continued for two or three weeks and not longer. Much must depend on the effect which a course of spa treatment has on the individual case, and the local physician must decide not only on the doses, but also on the duration of the course. There are cases in which it is wise to give small doses for a long period of time, and others in which it is more advantageous to give large doses for short periods only. In some instances two courses are required in the same year, with a longer or shorter rest between them. Again it frequently occurs that two courses of different waters ought to follow one another; for instance, in a case of anæmia with a sluggish portal system and passive congestion of the liver, it may be necessary to begin by a course of saline waters to unload the portal system, and afterwards to use chalybeate waters.

After-management. — The success of courses of mineral waters often depends entirely on the way in which the first three or six weeks following the treatment are employed. In almost all cases it is necessary to spend some time away from home at a good climatic resort, with careful diet and with open-air life, but without mental or bodily fatigue. It seems difficult for many people to see this, but we cannot too strongly advise our professional brethren to insist upon it. Some waters, like the simple thermal or thermal-sulphur waters, especially when taken at bracing localities, require a shorter after-treatment than the more complicated and searching waters of Carlsbad, Marienbad or Tarasp.

Every one who is acquainted with the "Weir Mitchell treatment" will admit that its author is correct in demanding after the termination of the treatment proper a further absence of six or eight weeks from the excitement and worry of home life; and some of us must have found that the neglect of this demand often destroys the good effect of the previous treatment. Similarly, after a serious course of waters the whole system is in many persons in an abnormal state of sensitiveness or unstableness, especially as regards the organs of digestion, circulation, and, not least, the nervous system. Injurious influences, however slight, such as a chill, mental or bodily fatigue or excitement, a mistake in diet, are apt to cause a new break down. We ought not to be influenced in our directions by the fact that some strong persons can do everything, even at or after Carlsbad, with impunity. Such cases form rare exceptions, not the rule.

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B. — HYDROTHERAPEUTICS

Under the term "Hydrotherapeutics" the therapeutic use of water is considered, especially in its external application to the body. The internal and external uses of natural mineral waters are dealt with in the article on "Balneo-therapeutics."

History. — Hydrotherapeutics was known to the ancient Greeks and Romans, and regular bathing of the body and keeping of the skin in a healthy condition were, like the athletic training of the body, held by them in high esteem. It is possible that a reaction from the excessive luxury of later Rome partly helped to bring baths into the neglect into which they fell amongst the early ascetic Christians.

In Italy and France hydrotherapeutics made a start in the fifteenth and early sixteenth centuries, and were even applied in mental diseases, as narrated in one of Poggio's tales. In the seventeenth century Floyer and T. Smith wrote on hydrotherapeutics in England, and in the early eighteenth century F. Hoffmann wrote on the subject in Germany. About the middle of the eighteenth century J. G. and J. S. Hahn treated febrile diseases with cold sponging, and one of them, when attacked with typhoid fever, had himself treated by this method, modifications of which have been so widely adopted in modern times. In the latter part of the eighteenth century, in spite of the results by W. Wright, James Currie and W. Jackson, and in Germany by Reuss, Frohlich, Brandis and Horn, hydrotherapeutical treatment was again falling into disuse, when, soon after 1820, Vincent Priessnitz, originally a small farmer of Graefenberg in Silesia, began to treat every kind of

ailment, chronic as well as acute, by hydrotherapeutic means. He added to the external applications the abundant internal use of water, and with this treatment he combined active exercise, and a very simple diet, and prohibited tea, coffee and all alcoholic beverages. Priessnitz at different periods made considerable alterations in his hydrotherapeutic measures. Originally he packed patients for several hours in dry woollen blankets, covered with feather beds, before applying cold affusions; later he substituted packing in wet linen sheets for several hours, followed by a full bath or a douche; still later he frequently employed a cold wet pack of fifteen or twenty minutes' duration, repeated several times in the same day. He introduced the method of rubbing the whole body with a cold wet sheet instead of the full bath; and made extensive use of partial baths for the hips, the hands, the arms, or the feet, of wet abdominal belts, and of wet applications on different parts of the body. The success of his measures, combined as they were with a simple diet and exercise in a healthy, mountainous country, was in many cases considerable; but the indiscriminate, too energetic, and protracted use of his methods often led to unfavourable results. The system was beginning to be regarded as a sort of quackery, when, about the year 1850, establishments were placed under the superintendence of regularly-educated physicians, who studied the physiological effects of the different methods, and modified them according to the requirements of individual cases: they also added pharmaceutical remedies when required. To the more modern works, by Winternitz, Hayem, Scheuer, etc., the writers of the present article are largely indebted.

Although England has taken such a prominent position in the use of baths in health, especially the daily morning "tub," it is remarkable that, as compared with French and German hospitals, the London hospitals are still very badly furnished with douches, and other means of hydrotherapeutic treatment.

Modes of Application. — Amongst these are the ordinary full bath at different temperatures, hip-baths, shower or rain baths, wrapping in wet towels, affusions, douches of various kinds, and many forms of local applications. The temperature may sometimes be varied during the application (alternating douche, Scotch douche). Among the many forms of medicated baths only a few can be mentioned here. Brine-baths, to imitate sea-baths, can be made by adding about 10 lb. of sea salt to thirty gallons of water. Alkaline baths of thirty gallons contain about six ounces of carbonate of sodium or three ounces of carbonate of potassium. Acid baths can be made by adding about twelve ounces of diluted nitro-muriatic acid to thirty gallons of water. The common bran and mustard baths need not be described. Aromatic and pine baths are made by adding a decoction of aromatic plants, such as lavender or fresh pine leaflets, or an extract or essence of pine leaflets to warm water. Mercurial baths belong to the treatment of syphilis, and electrical baths will be described under "Electro-therapeutics." Baths can also be made to imitate those of natural mineral waters.

The varieties of hydrotherapeutic application are very numerous, but most ends which can be attained in the present state of our knowledge can be arrived at by the judicious use of a very small number of appliances.

The internal use of plain water as a therapeutic agent, much employed in the old "water cure," is now generally but an adjuvant to other methods of treatment. Vapour and hot air baths may conveniently be classed with hydrotherapeutic appliances. In the Turkish and Russian baths the patient is placed in a chamber heated with watery vapour; but a vapour-bath may be taken in a box not including the head. In the Roman bath the hottest chamber, the "Calidarium" or "Sudatorium," is heated by dry air to a temperature of 133° to 140° F., and perspiration is more free than in vapour baths. These baths may be followed by soaping, rubbing, douching, and a plunge into cold water.

Treatment by hydrotherapeutic means depends chiefly on the reaction of the organism to cold and heat; but a mechanical stimulation is added to the purely hydrotherapeutic effect by the impetus of the water in douches, and to some extent by the bubbles of carbon dioxide in the waters of Schwalbach, Nauheim, etc.; the addition of a little mustard has a chemically stimulating effect, and a bran-bath diminishes the irritability of the skin; stimulation of the skin may also be increased by friction and massage. Care must, however, be taken that stimulation does not exceed the powers of the organism, and supervision by a medical man is necessary for the proper regulation of the treatment in every case. Each case must be individually considered, and hydrotherapeutic treatment may be associated, according to requirements, with change in diet, air, and the surroundings of the patient; or with a course of mineral waters or internal medication.

Action and Physiological Effects. — What has been called the "hydrotherapeutic reaction" is the natural reaction of the organism to cold or heat; the organism thus endeavours to defend itself against the action of these agents. In human beings, the skin of the body, unprotected by any natural covering, reacts the more readily to cold and heat; in most races this sensitiveness is increased by the habitual use of clothes: the clothes form a sort of zone around the body, in which the temperature stands, with tolerable regularity (according to Winternitz) at about 90° F. In order, therefore, to obtain the "hydrotherapeutic reaction" it is necessary that the water should have a temperature some degrees above or below 90° F. It is obvious, also, that on account of its greater specific heat and greater coefficient of heat conductivity, water is much more active than air of the same temperature in inducing the reaction. On the proper bringing about of this reaction the result of hydrotherapeutic treatment largely depends.

Cold Water Treatment. — When a healthy man jumps into a cold bath, or has a cold douche applied over the whole or a considerable area of his body, he receives an impression of cold, shivers, and, after an almost involuntary pause in breathing, takes a very deep inspiration. The skin is pale, and owing to the contraction of the unstriped

muscle fibres, presents the appearance called "goose skin." When the man gets out of the bath, or sometimes even whilst he still remains in it, these first effects give place to the phenomena of the "reaction." The skin then becomes slightly reddened, and an agreeable subjective sensation of warmth is experienced. He breathes more easily, and has a general feeling of comfort and capability for exertion. This is the "hydrotherapeutic reaction" to cold; it depends in degree and rapidity on the temperature of the water, the length of the application, and, in the case of a douche, on the force with which it is applied. The reaction is assisted by voluntary movements and friction of the skin, and varies much with the health and strength of the individual and with his previous habits in respect of cold bathing. To those already accustomed to cold baths the initial shock is not unpleasant, and the reaction sets in much more easily.

Many physiological experiments have been made to explain scientifically what takes place when the whole body is exposed to cold. The pallor of the skin during the initial shock is due to the contraction of the superficial blood-vessels, which sets up a corresponding dilatation of the internal vessels of the body. As the blood is the great distributor of heat in the body, the central temperature, measured by a thermometer in the rectum, may rise slightly at first. The contraction of the superficial blood-vessels of the body must prevent excessive loss of heat until heat production is increased. Owing to this contraction of the superficial blood-vessels the general blood pressure rises and the heart's action is increased.

When the reaction sets in, the superficial vessels dilate, the flow of blood through the skin is much increased, and affects the sensory nerve terminations so as to give rise to a sense of warmth in the skin. Accompanying the reaction a thermometer in the rectum shows a slight lowering of the central temperature, which then gradually regains its initial level or slightly surpasses it.

The vascular phenomena consequent on the hydrotherapeutic application are clearly proved to be due mainly, if not entirely, to nervous vaso-motor action; for, although the muscular walls of the arterioles, like other unstriped muscle, can certainly react to direct stimuli, the phenomena follow a stimulus too fleeting to act directly on the muscle fibres (Hayem). The phenomena are not, to any considerable extent at least, due to the peripheral nervous mechanism, but to a reflex mechanism including the central nervous system: in animals they are absent from parts in which the nerves have been experimentally cut; and in the case of men the phenomena may be diminished or absent in paralysed and anæsthetic limbs. An attempt to trace out the "reflex arcs" concerned in the hydrotherapeutic reaction would take us too far away from practical medicine.

The respiratory phenomena observed after the application of cold water to the skin are also due to a nervous (reflex) action; they have been produced in animals rendered insensible by chloral (Roehrig).

These phenomena consist in increased amplitude of the respiratory movements, with increased liberation of carbon dioxide and absorption of oxygen by the blood circulating through the pulmonary capillaries.

Increased combustion in the tissues is due to the need for increased heat production to compensate the heat given up to the cold water. Shivering must be regarded as part of the means whereby nature causes increased heat production. As is the case during muscular exercise, this increased combustion is shown by the increase of carbon dioxide given off by the lungs. Increase of urea and diminution of uric acid are sometimes observed in the urine of patients under hydrotherapeutic treatment; and, when observed, show that the nitrogenous catabolism in the body is more extensive. When, owing to the continued application of cold, the muscular layer of the body becomes cooled catabolism is diminished, but it is again increased when the reaction takes place after the application.

The flow of urine is increased and the action of the bowels promoted, the latter probably being due partly to increased peristaltic action, partly to increased intestinal secretion. The appetite is stimulated, the digestion of food aided, and the tonic effects on the nervous and muscular systems increase the desire for physical exertion and make work feel lighter.

If the cold application (douche or bath) instead of being general, be *local*, and especially if it be limited to an extremity, the general effects are less marked. Local applications have been shown, however, to cause certain distant reactions. Thus, when iced water is applied to one hand both become colder, and both show a diminution in volume as measured by the plethysmograph. These phenomena are doubtless due to the diminution in the amount of their blood, caused by contraction of their blood-vessels. Inverse phenomena are observed to take place at a level of the body remote to that affected by the cold application; thus, during the application of a cold hip-bath, Winternitz has found that an augmentation in the volume of the arm takes place. These distant reactions following on local applications form an additional argument in favour of the reflex nature of the general "hydrotherapeutic reaction." If an antiphlogistic action be desired, it is important that the local application of cold be continuous: Leiter's tubes are less easily displaced than icebags.

Warm Water Treatment. — Whereas the chief ultimate effect of cold stimuli to the skin is tonic, that of warm stimuli is sedative. The effect of the warm treatment is not, however, exactly the opposite of that of the cold; indeed, all cutaneous stimuli whether mechanical (by friction or massage), electrical (by faradic shocks), chemical (by counter-irritants), or thermic (cold or hot), show certain points of analogy.

Like cold applications hot ones probably produce an initial vasocontraction; this, however, passes off quickly and gives place to vasodilatation, which lasts during the rest of the application, and then slowly

passes off. This dilatation of the superficial vessels, with the subjective feeling of warmth, is the characteristic effect of hot applications. The superficial vaso-dilatation is associated with increase in the secretion of sweat and in the frequency of the respiratory movements. The whole constitutes the reaction of the body to heat, and thus the animal mechanism increases the loss of heat to counteract the heating effects of the application. Owing to superficial vaso-dilatation more heat radiates from the body; by increased sweating the loss of heat by evaporation is augmented; and by increased respiratory movements more heat is given off in the air and watery vapour expired.

In addition to the local sedative action of hot applications on the sensory nerves, as seen in the application of poultices and hot fomentations, there is a general sedative action exercised by heat, when the application is general and sufficiently prolonged. This general sedative action is shown by diminished desire for exertion, and is probably explained by the partial emptying of the deeper blood-vessels and slowing of the blood-streams which accompany the dilatation of the superficial vessels, and cause a certain anæmia of the viscera and brain.

If the loss of heat be partly prevented by immersing the whole body in a bath of hot water, the central temperature, as measured by a thermometer in the rectum, rises somewhat; but doubtless in such cases diminution of the heat production in the body assists the loss of heat by respiration to prevent undue rise of the body's temperature.

Hot applications tend to constipation. This may, perhaps, be due to diminished peristalsis, perhaps to a diminution in the intestinal secretion on the increased excretion of sweat.

The local applications of hot water, like local cold applications but to a lesser degree, have been found to cause certain distant reactions. Thus when one lower limb was heated, vaso-dilatation, increase in volume, and sweating were observed in the other lower limb.

Hot air and vapour baths differ from hot water baths chiefly in their action on the skin; the greatest amount of perspiration is obtained by hot air baths.

The Internal Use of Water. — Plentiful drinking of water leads to increase in the watery secretions; besides the urine, the bile, saliva, pancreatic juice and sweat appear to be increased; though if increased secretion of sweat be desired, it is generally stimulated by heat or bodily exercise. This increase in the watery constituents of the secretions is accompanied, for a time at least, by increased excretion of the waste products of tissue metabolism, which are "washed out" from the tissues and the blood itself. The effects of plain water taken internally form a considerable part of the results obtained from courses of mineral waters (see article on "Balneo-therapeutics"), and the treatment may exercise a good influence in some cases of gout, urinary gravel, imperfect secretion of bile, and constipation from sluggish peristaltic action. Excessive water-drinking, on Priessnitz's original plan, may however lead to dyspepsia.

Diseases and Morbid Conditions Suitable for Hydrotherapeutic Treatment

Digestive Derangements. — Habitual constipation from atony of the bowels, often associated with a tendency to hæmorrhoids and "abdominal venosity," may sometimes be treated with cold baths and other stimulating methods, which increase the general nutrition of the tissues and the physical and psychical energy of the nervous system. In cases of chronic dyspepsia with catarrh of the stomach the common salt waters and alkaline sulphated waters (as at Carlsbad) are more frequently used and often preferable; but hydrotherapeutic treatment may be employed for the tonic after-treatment, or it may be employed with due care from the beginning as an adjuvant to the other treatment.

Muscular Pains and "Muscular Rheumatism." — Some of these cases may be treated with cold, some with hot baths, or with hot air or vapour baths, according to the patient's power of reaction; they are often treated by warm or hot baths followed by a cold shower bath. The diaphoretic methods by packing with woollen blankets or wet sheets are often found to be useful, but they sometimes fail. In this class of cases the original supporters of hydrotherapeutic treatment considered their methods infallible, but this is by no means the case. Invalids of this class should not be exposed to all weathers during the cure, and the access of cold air to the wet body should not be risked. The course of treatment should not be too prolonged at one time, but may be repeated again after an interval of some months: the interval may advantageously be spent at sheltered sea-side localities, at moderate elevations, or at one of the gaseous thermal saline spas.

Sciatica and Neuralgias. — Some patients may be treated by hot baths, but they are more often sent to natural thermal spas, such as Schlangenbad, Wildbad, etc.

Hepatic and Nephritic Colics, etc. — Hot baths may be of great service in hepatic and nephritic colics, probably by the relaxing action on unstriped muscle, and in helping the action of opiates. They may sometimes be of service in severe flatulent colic, in tenesmus, in retention of urine, etc.

Rheumatism and Gout. — In chronic rheumatic joint affections the patient is often too enfeebled for cold hydrotherapeutic treatment, but a hot bath (with the help, if necessary, of a chair to lower the patient into the bath), may be useful in the treatment of such cases. Mild cases of gout may derive benefit from the usual hydrotherapeutic treatment, in so far as it aims at invigorating the nervous system, and producing more complete oxidation of the downward products of tissue metabolism; the treatment should be associated with moderation in the amount of food, and especially in the use of stimulants. Local packing may cause fits of gout, and indeed the hot mustard foot-bath has been used for this purpose in supposed cases of "suppressed gout." The more severe forms of gout

are too much complicated with general constitutional defects to encourage us in recommending cold water treatment.

Catarrhal Attacks. — Weakness or over-sensitiveness of the skin, or nerve terminations in the skin, may be the cause of frequently recurring attacks of diarrhœa, or of tendency to catarrh of the respiratory mucous membrane; at all events, when this over-sensitiveness is present, cold is more likely to induce such attacks. Hydrotherapeutic methods, mildly stimulating at first, with gradually increasing energy, are here useful; unless, as in impeded convalescence, the reactive power is so reduced that gaseous thermal salt baths and mountain air are preferable. In some cases sea-air and sea-baths are most useful.

Chronic Affections of the Skin. — In local perspirations, some cases of prurigo, and chronic affections of the skin, hydrotherapeutic treatment in a modified form may be useful; it may also be used as an adjuvant in the treatment of syphilis. In some affections of the skin alkaline baths are of service, and bran-baths are used to allay cutaneous irritability. Psoriasis has been successfully treated by prolonged cold baths.

Chronic Metallic Poisoning. — In some cases of this sort, if there is sufficient reactive power, cold water treatment may be of as much good as the thermal sulphur treatment. The treatment will be aided by the abundant internal use of water, and if necessary by the administration of iodide of potassium, which is commonly supposed to assist in the removal of the poison from the tissues.

Hysteria, etc. — Cold water treatment, pine-baths, and aromatic-baths may sometimes be found useful in the treatment of hysteria and functional nervous affections, and in some cases of "diabetes insipidus." In organic nervous diseases they are not to be recommended, unless it be to relieve the lightning pains of tabes.

Catamenial Irregularities. — These are frequently treated at hydrotherapeutic establishments. Profuse menstruation may often be checked by the regular use of the cold hip-bath for three to five minutes. In cases where the menses are insufficient, warm hip-baths of ten to fifteen minutes' duration, combined in some cases with wrapping in a wet sheet, may often be found useful; dysmenorrhœa is likewise occasionally treated with advantage by the partial wet sheet or hot baths.

Anæmia. — Scheuer recommends the treatment of some anæmic conditions by hydrotherapeutic measures. Under general cold applications an increase in the hæmoglobin and number of the red blood corpuscles has been observed. Of course special care must be observed in the treatment by cold water of anæmic and feeble persons. According to Scheuer the loss of heat can be counteracted by rest in bed, by wrapping up after the application of cold, by preliminary moderate exercise, or by previously over-heating the body in the hot air chamber, or by hot water, as in the Scotch douche.

Rickets. — In some rickety, scrofulous, and other ill-nourished children regular bathing in rather cold salt or sea water may form a part of the treatment, provided that great care be taken to avoid a chill.

Infantile Convulsions, etc. — Hot baths of short duration, with or without the addition of mustard, are often employed for the immediate treatment of laryngismus stridulus and general convulsions in children. Hot baths also are sometimes used for adults in cases of puerperal eclampsia and uræmic convulsions, but in these cases some benefit is expected from their diaphoretic action as well as from their sedative influence on the cerebrum. Cold douches, or the continuous application of cold (by some form of "cap"), to the head are often of the utmost value in acute delirium; as for example in the course of the infectious fevers. Delirium and screaming are sometimes arrested almost at once by holding the patient's head over a pail at the bedside and pouring cold water over the head, beginning near it and slowly raising the can higher and higher.

Nephritis and Uræmia. — The wet pack, hot water, hot air, or vapour baths are sometimes of service by producing diaphoresis. When the patient has to remain in bed the application of the two latter baths requires especial care.

Enteric Fever and other Acute Infectious Diseases. — Of acute febrile diseases enteric fever is the one in which cold baths have been most practised. Brand's direction for the use of the cold bath is in general to take the rectal temperature every three hours; if it be 102·2° F. or more, the patient is to be placed in a cold bath of 64·4° F. to 68° F., and to be kept there until a slight shivering is observed, probably about a quarter of an hour. There are, however, many varieties of this treatment; English physicians, following von Ziemssen, prefer to place the patient in water at about 90° F., and to cool the bath gradually by the addition of cold water until the fever is reduced to about 101° F. Von Ziemssen's method is within fifteen minutes to cool the bath down from about 95° to 68° F.; the skin is lightly rubbed, and in 20–30 minutes, or when shivering commences, the patient should be put back to bed. His temperature usually falls one or two more degrees after removal to bed, which should be warm and contain a hot bottle for the feet. Cold affusions, cold sponging, the application of ice to the body, or the suspension of ice in vessels in a "cradle" within the bedclothes, have been used in milder cases for a similar purpose. Persistent fever in children may be conveniently reduced by filling wide-mouthed pickle-bottles with ice, wrapping each in flannel, and placing more or fewer of them about the patient — in the axillæ, against the flanks, or between the legs. Bottles may be added or removed from time to time as the thermometer may indicate. The temperature should not only be taken soon after the bath, but also after an interval of fifteen minutes; the temperature then indicates whether the bath was sufficiently cold; this indication is of use in regulating the next bath. A little alcohol may be administered before or whilst the patient is in the bath, and friction may be applied to prevent the too sudden contraction of the cutaneous vessels. The use of cold baths in enteric fever was introduced by F. Glénard in 1871 from Germany into France, and was adopted

especially in Lyons. Dr. Osler, in the report on typhoid fever (*Johns Hopkins Hospital Reports*, vol. iv. 1894), speaks in favour of the bath method of treatment, which indeed has been widely practised in most countries, and is very efficacious, not only as regards the pyrexia, but in low delirium, subsultus tendinum, tympanites and like "typhoid" states. Similar methods have been used for acute infectious diseases other than enteric — in the typhoid symptoms sometimes occurring during the course of pneumonia, small-pox, erysipelas, scarlatina, etc. On account of the tonic and diuretic action of the baths, it is said that they may be employed also with advantage in some cases of infectious fevers, where, although the temperature is not much more than 100° F., a condition of prostration and tendency to stupor is found. Further details will be found in the elaborate account by Dr. H. Faure-Miller (*Les Bains Froids dans les Formes Typhoïdes des Maladies Infectieuses*, 1893).

Hyperpyrexia. — In cases of hyperpyrexia, occurring in the course of acute rheumatism and other acute diseases, the advantage of the cold water treatment over the internal use of antipyretic drugs is now generally admitted, and the methods of its use are well understood.

Burns, Phlegmons, etc. — The use of baths for these cases comes under the head of surgery.

Contra-Indications. — For the successful results of cold water treatment it is essential that the organism be able to stand a certain amount of abstraction of heat; that it be capable of more or less energetic reaction, and that the digestive and assimilative organs be able to take up a fair amount of nourishing material to compensate increased catabolism. In cases of great debility after illness special care must be observed, and cold water treatment is still more hazardous when, to the debility of illness, the weakness of childhood or old age is added. When cold water treatment causes diarrhœa, urticaria, or hæmoglobinuria, it must be discontinued; and in chronic nephritis and any great degree of arterio-sclerosis it is contra-indicated; so also is it certainly in cases of aneurysm, in those who have had one attack of cerebral hæmorrhage, or appear threatened with cerebral hæmorrhage, and in all cases of heart disease, except in slight and well-compensated mitral valvular affections. The abundant use of liquids internally is injurious to patients with old valvular heart disease and a tendency to loss of compensation; it is to be avoided likewise by many obese persons with weakly acting hearts.

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THE MEDICAL APPLICATIONS OF ELECTRICITY

Although a large number of books have been written upon medical electricity its use makes slow progress among medical men. The apparent reasons for this are that the apparatus is expensive, its management troublesome, and the time required to carry out the treatment more than a busy practitioner can spare; these objections would probably vanish quickly if the fact could once be grasped that electrical treatment is of real value in a considerable variety of cases. The true

reason for the slow advance of medical electricity is that the medical profession have not yet become fully aware of its advantages.

There is no manner of doubt that electrical currents produce definite physiological effects; from a consideration of these it is possible to arrive at an estimate of the value of electricity in the treatment of disease, and medical electricity may be defined as the application of our knowledge of these physiological actions to the study and treatment of disease.

The most obvious physiological action of electricity is its power of stimulating living tissues. This is apparent enough when the current is applied to nerves or muscles, for it can be felt and seen: but the stimulating effect is not confined to nerves and muscles; it can also be observed in unicellular organisms, and its results noted in several ways in man and animals. The metabolic activity of the tissues can be considerably increased by electricity, as Gautier and Larat have shown in their experiments upon the elimination of carbonic acid gas and urea under electrical treatment, when it was found that an increase of 40 or 50 per cent could be produced by general electrification. This trophic action of electricity has valuable applications in medical treatment. It is surprising to see the great improvement in general health shown by children during a course of electrical treatment for infantile paralysis; and in rickety children the most encouraging results have been obtained. The same beneficial trophic effects are commonly seen in adults; and the most suitable methods of treatment will be considered below under the head of general electrification. In addition to the other methods of improving nutrition — such as change of air, exercise and gymnastics, massage, or the administration of cod liver oil and certain other drugs — we have in electricity a most direct and useful means to the same end, and one which sometimes offers advantages over all the others.

When the question is one of localisation of the stimulating effect, then the advantages of electricity are conspicuous, as is clearly shown by the almost exclusive use of electrical methods by physiologists when local stimulation is required for purposes of experiment. The power of exercising and of stimulating to contraction any paralysed muscle or group of muscles is a most valuable one.

The electrotonic effects of currents can also be applied to purposes of treatment. By **electrotonus** is meant the changed condition of a nerve during the passage of a steady current through it; that is, an increase of irritability in the region of the negative pole, and a decrease round the positive pole. Physiological principles suggest the use of the anode (or positive pole) for conditions of exalted irritability, such as neuralgia or spasm; and the use of the kathode for paralytic or paretic states: thus we are often enabled to obtain favourable results. In patients with injuries to nerves and impaired cutaneous sensibility the electrotonic effects of the current are often plain enough; the application of the anode to the affected region with a moderate current may be able to abolish all sensibility for the time, while the use of the kathode will

restore it in an increased degree. So too it is common for a trigeminal neuralgia to fade away completely during the application of the anode over the affected region, and it often happens that a neuralgic pain thus dissipated does not return.

Another effect of the current is **electrolysis,** which is made use of in surgery when destructive effects are desired; as, for example, in the treatment of nævus. In medical treatment these destructive electrolytic effects at the surface of the electrodes have to be remembered in order to be avoided; but the electrolytic process implies not merely the dissociation of chemical compounds at the poles, but also a rearrangement of the molecules composing the electrolyte which lies between the poles — *i.e.* in the case of the body, the juices and tissues: and it is not impossible that some of the results of electrical treatment may be due to interpolar electrolytic actions in the tissues traversed by the current. It is difficult at present to estimate the exact importance of these molecular changes, but they may be considered for the present as "alterative" effects.

Sometimes it is possible to make use of a peculiar property of electric currents as a means of introducing drugs into the system through the skin; the process of **electric osmosis or cataphoresis** causes the passage of solutions from the positive to the negative pole, and many applications of it have been suggested, such as the direct introduction of iodide of potassium into a syphilitic node or gumma, or the elimination of metallic poisons from the system. Its chief value, however, may consist in the production of local anæsthesia of the unbroken skin by cocaine: this can readily be done by placing on the skin a few thicknesses of blotting paper wet with 10 per cent cocaine solution and applying the positive pole over it, the circuit being completed through the body to the negative pole placed on some remote part. With a moderately strong current of five to ten milliampères the skin can be rendered anæsthetic in five minutes.

The phenomena of electrotonus, of electrolysis, and of electric-osmosis are peculiar to the direct current; the stimulating and trophic effects belong both to direct and to alternating currents, though they are more apparent with the latter.

In medicine both the direct and the alternating current are in daily use; the consideration of what has just been written will serve as a guide in the choice of one or the other for the treatment of particular cases. Fashion has had no little influence in deciding the preference of one or other of these electrical methods.

The apparatus required for electrical treatment and diagnosis is in reality a simple matter, although the elaborate catalogues of the instrument makers are apt to give the idea that it is rather complicated. The words Franklinism, Galvanism, and Faradism will not be used in this article; but in their place I shall speak of electrostatic methods, of treatment by the battery current, and of treatment by the induction

coil current. **Electro-static treatment** consists in the use of charges from an electrical machine of high potential, with sparks, the brush discharge, or the discharges of Leyden jars. These electro-static methods were applied to medicine almost on their discovery; and the early writers on medical electricity enumerated long lists of cures effected by their means; these old records, however, hardly repay a study, partly because many of the patients seem to have been hysterical, while the others are so described as to make it difficult to diagnose the respective diseases. After the discovery of the voltaic pile the use of the electrical machine gradually fell into disuse; but it is now being revived with modern apparatus and a better knowledge of the subject. In France especially these methods have been much in vogue during the last few years, and a certain amount of scientific work has been devoted to them, so that we are beginning to gather some little trustworthy knowledge of the physiological effects of high potential electrification. There seems to be no doubt that in this way certain general nutritive changes can be brought about; the effect on healthy persons probably being to increase the metabolic activity of the tissues, and in some cases to such an extent as to do harm. Thus, in some careful experiments upon himself, Truchot found that as a result of a course of electro-static treatment a feverish state of body was produced, with accelerated pulse, raised temperature, and increased elimination of nitrogen. In certain morbid states this increase of activity seems to be useful, notably in people of a torpid condition of body, in the anæmic, the debilitated and the convalescent. These effects have been noticed from the simple electro-static charge. When sparks are combined with this certain local effects may be superadded, and with Leyden jars forcible muscular contractions also occur. The whole of this branch of medical electricity requires fresh investigation on physiological lines, and much which was written by the older writers requires to be forgotten. The clinical gains have been in the treatment of some skin diseases, especially eczema and eczematous ulcers; the removal of certain states of abnormal obesity; the relief of neuralgia, and so on. Moreover, electro-static methods have above all the power of combating many hysterical manifestations, such as pains, anæsthesias, contractures and paralyses: these last, however, depend rather upon the psychological than on the physiological effects of electricity. In this country, unfortunately, electro-static methods of treatment have not yet received proper study, and are generally regarded as having no effects except through the mental impressions produced by the treatment; but there is probably more of value in them than is yet believed.

The best type of electro-static machine is the Wimshurst machine; and it is advantageous to use one with eight or twelve plates, each having a diameter of twenty inches, and to enclose the whole machine in a roomy glass case to protect it from the dust which is abundantly attracted by the machine when in action. Details of management must be looked for in the special handbooks.

For carrying out the methods in ordinary use with *battery and*

induction coil, it is perhaps best at the beginning to procure a portable combined battery from a good maker. This can be used either in the consulting room or in the patient's home, and is therefore superior to a fixed installation. It is unwise to multiply batteries; they gradually deteriorate with keeping, whether used or not, and it is easier to bear the expense of maintenance of one battery than of two or more. The combined battery should consist of twenty-five or thirty small size Leclanché or "dry" cells, with a current collector or switch for progressively taking cells up into circuit one by one; a galvanometer graduated in milliampères; a commutator for reversing the direction of the current in the external circuit; a pair of binding screws for the attachment of the conducting wires; an induction coil with one or two separate and larger sized cells to drive it, and a key for switching on either the induction coil current or the battery current to the terminal binding screws at will. Some mode of regulating the strength of the induction coil is necessary.

Such an apparatus can be had at prices varying from eight to fifteen pounds, and is the most convenient arrangement for all medical purposes of testing and treatment, though it is not suitable for the large currents needed for galvano-cautery or for instruments with electric lamps. A pair of flexible conductors of insulated wire and a few electrodes make up the outfit. It is best to procure any special electrodes as occasion arises: those wanted for general purposes are of two kinds, — one a flat pad of metal, oval, four inches long, covered with wash-leather or amadou, and fitted with a binding screw; and the other, a handle to which metal discs ranging from half an inch to two inches in diameter can be attached. The former is called the indifferent electrode; during treatment it is applied to some indifferent part of the patient's body, where the pressure of the clothes usually suffices to keep it in place — on the back of the neck, for example, on the sternum, or the sacrum. The other or active electrode is manipulated over the region affected. For testing the nerves and muscles it is convenient to have a special electrode fitted with a key for closing the circuit at will.

A sheath for the indifferent electrode with one side waterproof is convenient, as it protects the patient's clothing from being wetted. It is important to have clean coverings for the electrodes; and so far as possible to provide each patient with a separate electrode and sheath; a handy form of electrode is made in which the wash-leather covering can be changed in a few moments. Salt water is not necessary for the moistening of the electrodes, and, as it corrodes them more rapidly than plain warm water, the latter is to be preferred. The silk covered conducting cords should be light and flexible, four or five feet long, and of two colours, to distinguish their attachments the more easily.

Units of Measurement. — It is impossible to have clear ideas upon medical electricity unless the meaning of the words Volt, Ohm and Ampère are understood. These terms stand for the units in which electrical quantities are expressed, and are as necessary to the subject as are the better known units of measurement, such as the inch, the pound

and the pint, to matters of everyday life. The *volt* is the practical unit of electro-motive force, or electrical pressure; and the electro-motive force of a battery expresses the tendency of such a battery to produce an electric discharge, just as the pressure in a steam-boiler signifies the tendency of the boiler to emit steam; in the former case the closure of a conducting circuit, and in the latter the opening of a valve is necessary to cause the discharge.

The *ohm* is the practical unit of resistance, and is necessary because electrical conductors differ from one another in their specific conductivity; those which conduct well are said to have a low specific resistance, and those which conduct badly are said to have a high resistance. Metals are good conductors; and of metals silver and copper have the least resistance. The resistance of a wire or rod or other mass of any substance depends upon the specific resistance of the substance, and varies directly as its length, and inversely as its sectional area or thickness: thus a long or a thin wire of copper will have a greater resistance than a short or thick one. The *ampère* is the unit of current, and the three units are so related to one another that an electro-motive force of one volt acting upon a conductor with a resistance of one ohm will set up in that conductor a current of one ampère. This relation, known as Ohm's law, can be expressed, in symbols, by $C = \frac{E}{R}$, where C stands for current, E for electro-motive force, and R for resistance: if two of the three quantities are known the third can be calculated from them; thus when an electro-motive force of 12 volts act upon a resistance of 8 ohms, $C = \frac{E}{R}$, or $C = \frac{12}{8}$, or $C = 1{\cdot}5$ ampères, which is the resulting current.

As a current of one ampère is never applied to patients in medical treatment, the thousandth of an ampère (·001 ampère) or milliampère forms a more convenient unit, and medical currents are usually expressed in milliampères; thus five milliampères is a common magnitude of current, and it is more easily expressed in that way than by the fraction ·005 ampère.

The resistance of the body is high, very much higher than that of a metal; and it varies considerably with the moisture or dryness of the skin: under conditions of medical treatment with wetted electrodes, it may be taken as ranging between 1000 and 5000 ohms. It is worth while to calculate the electro-motive force necessary to send a current of five milliampères through such a resistance. First, in the case of 1000 ohms—

$$C = \frac{E}{R} \quad \therefore \quad RC = E$$

$$R = 1000 \quad C = {\cdot}005. \qquad E = 1000 \times {\cdot}005 = 5 \text{ volts.}$$

Secondly, in the case of 5000 ohms—

$$E = RC = 5000 \times {\cdot}005 = 25 \text{ volts.}$$

A medical battery must therefore have an electro-motive force of twenty-five volts if it is to drive a current of five milliampères through a body whose resistance is 5000 ohms.

The Leclanché cells usually supplied in portable batteries have an electro-motive force of 1·5 volts per cell; thirty cells (a usual number) properly connected together have a combined electro-motive force of forty-five volts: this gives an ample margin, and would send a current of fifteen milliampères through a resistance of 3000 ohms. As this current is very rarely exceeded, and as, by thoroughly moistening the skin, the body resistance can usually be brought well within 3000 ohms, this number of cells is sufficient. Beyond this the weight and cost of the battery increases out of proportion to its efficiency. The current from the cells of the battery flows through the circuit in one direction from the positive to the negative terminal, and, so long as the circuit is closed, with almost unvarying strength; when it is broken, by removing the electrodes from the patient or by opening a key in the circuit, the current ceases abruptly. If the electrode be caused to slide over the surface of the body there will be variations in the lines of flow in the neighbourhood of the moving electrode; and the point of entry of the current, or point of greatest density of flow, will vary in position, even though the total current flowing in the circuit, as indicated by the galvanometer, be steady and uniform.

The current from the **induction coil** is of a different kind, inasmuch as its strength is continually varying with the electro-motive force of the coil which rises and falls in the form of a wave with each vibration of the moving contact breaker; each rise and fall of electro-motive force means a rise and fall of the current through the circuit. If the *primary coil* of the induction apparatus be used the consecutive waves of current are all in one direction; if the *secondary coil* be used they change or alternate in direction. In medical coils the current of the primary circuit is not always adapted for use, and it has no therapeutic advantages over that of the secondary coil; the secondary current is a current alternating in direction about fifty times per second and wave-like in character; that is to say, it rises from zero to a positive maximum, then falls away again to zero, rises to a negative maximum, and again returns to zero; each electrode is thus alternately positive and negative. There are several ways of regulating the strength of the secondary coil: one of the best is by winding it on a separate bobbin which can be made to slide between guides so as to vary its position in the magnetic field of the primary coil; as the secondary is withdrawn from the primary the current becomes weaker, and *vice versa.*

The measurement of the alternating currents of the induction coil (which do not affect an ordinary galvanometer needle) has been for a long time a serious difficulty, and, in electrical testing, comparisons have been usually made by the aid of an arbitrary scale marked along the slide of the coil; this does indeed enable the relative positions of primary and secondary coils to be reproduced at will, but is of very little use in com-

paring the results obtained with two coils which may differ. Now at length an instrument is made which gives readings of the induction coil currents in milliampères, and as soon as its use becomes general our knowledge of the actions of the induction coil current will be placed upon a surer basis. Different instruments differ much in the painfulness of the sensation to which they give rise. In few of them are the successive discharges sufficiently equal to produce a smooth sensation. In the choice of a coil this point should be attended to, and pains should be taken to obtain one which has a contact breaker working smoothly and evenly.

The least painful rate of vibration is from sixty to a hundred impulses per second.

The properties of the discharges of the induction coil are modified by the number of turns of wire in the secondary windings. A coil of few turns (two or three hundred) has a lower electro-motive force and a lower resistance than a coil of many turns (two or three thousand); and besides its resistance there is another factor which increases with the number of turns, and is known as its self-induction: this retards the rate of rise and fall of current in the coil, and diminishes the magnitude of the current which can be taken from it. Thus a coil of many windings has a high electro-motive force so long as very small currents are taken from it, but this falls rapidly when the resistance of the external circuit is low; a short coil has a lower electro-motive force, but is capable of giving a proportionately larger current without fall in its electro-motive force. For treatment with moistened skin and wet electrodes a long coil is not needed, but for the stimulation of the superficial cutaneous nerve endings with a dry skin and a wire brush — a method sometimes adopted — a long coil is needed, as the dry skin has a very high resistance, and requires a high electro-motive force to drive through it even the small current required in this mode of treatment. Some medical coils are therefore provided with two interchangeable secondary coils; but the same advantage can be had from one coil, if its windings can be tapped so as to use either a part or the whole of it at will.

Too much has been made of the various qualities supposed to be obtained by varying the thickness of the wire and the numbers of turns in the winding; the rise and fall of the wave of current is rather more gradual from a long than from a short coil; this difference and the point mentioned above — that a long, fine wire is the best for stimulating the dry skin — give the pith of the matter. Recently very rapidly vibrating contact breakers have been advocated, because of a peculiar benumbing effect upon the cutaneous nerves which is produced by them. These, however, are not often useful.

Nerve and Muscle Reactions. — There is a marked difference in the way in which nerve and muscle respond to the battery current and the coil current respectively; and this has been made the basis of the electrical testing of nerve and muscle. In health the battery current produces a single twitch of a muscle when the circuit is closed, and another when the circuit is opened. In the interval between closure and opening

the muscle is quiescent, although the muscle or its motor nerve is being traversed by the current; the minimal current necessary to produce the contraction when the negative electrode is most favourably placed over a superficial nerve trunk is about one milliampère. With the positive pole

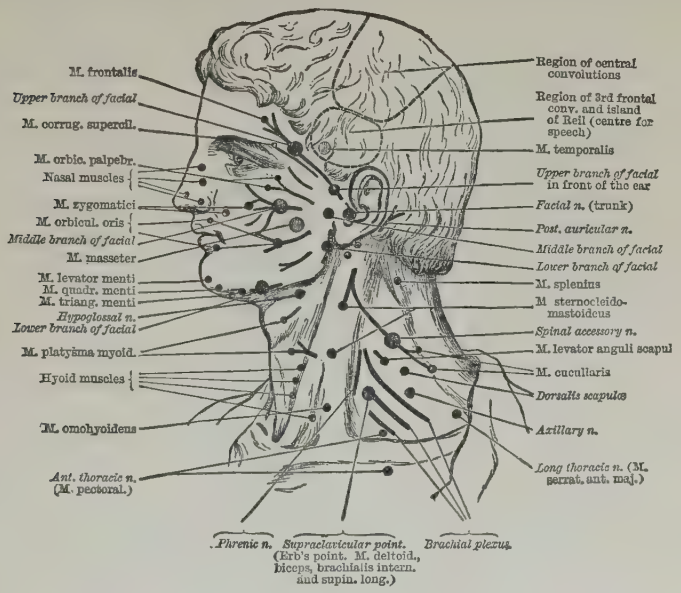

FIG. 26. — The Motor points. The Head and Neck.

a current of about twice the strength is needed, and in both cases the contractions are more easily produced by closure than by opening of the circuit. Thus there are four possible ways of causing a contraction: —

1. Closure with Kathode on the nerve or muscle, KCC, Kathodal closure contraction.
2. Closure with Anode ,, ,, ,, ACC, Anodal closure contraction.
3. Opening with Anode ,, ,, ,, AOC, Anodal opening contraction.
4. Opening with Kathode ,, ,, ,, KOC, Kathodal opening contraction.

These are arranged in the order of their appearance in health. In disease the order may be modified.

When the currents are stronger the muscle is not quiescent during the steady passage of the current, but is in a state of imperfect tetanus, which is called *closure tetanus.*

With the induction coil current the muscle passes into a state of tetanus, and remains so during the passage of the current. This is what

one would expect from the continual change of strength of the induction coil current, which acts as a rapid succession of separate stimuli.

These muscular contractions are obtained either by stimulating the motor nerve trunk at any part of its course, or by stimulating the muscle by placing the electrode directly over it. But even in this latter

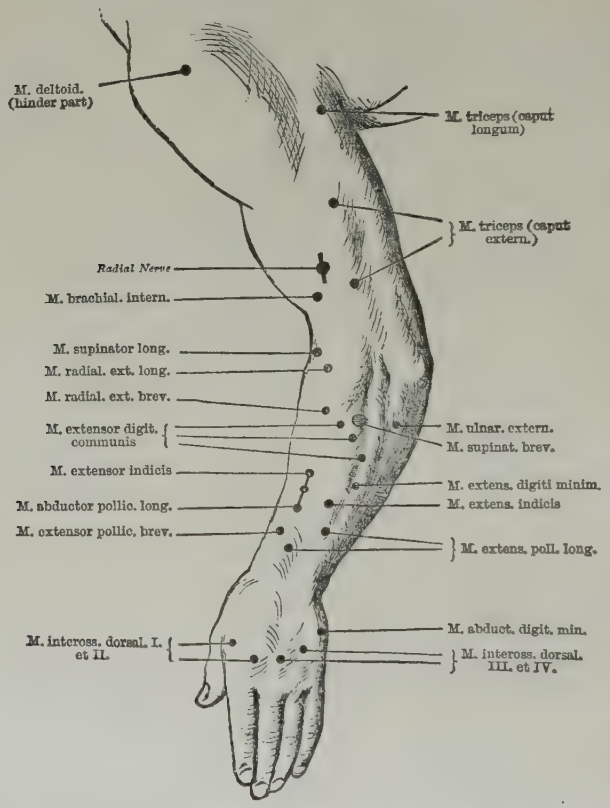

FIG. 27. — The Motor points. The Extensor Aspect of the Upper Limb.

case the stimulus is still distributed through the muscle by means of the ramifications of its motor nerves, which convey the stimulus more rapidly than the muscle fibres could do it.

In certain forms of paralysis the reactions become altered and the following condition is found: the motor nerve responds neither to the induction coil nor to the battery current; the muscle does not respond to the direct application of the induction coil current, and to the battery current it responds in an altered way, viz., the contractions at closing and opening the circuit produce a slow, sluggish contraction instead of the sudden twitch seen in health; often, too, the anodal closure proves a

more effective stimulus than the kathodal. These contractions (sluggish) may be produced by very small currents, or, on the contrary, strong currents may be needed to produce them. The irritability of the muscle to battery currents (galvanic irritability) is said to be increased

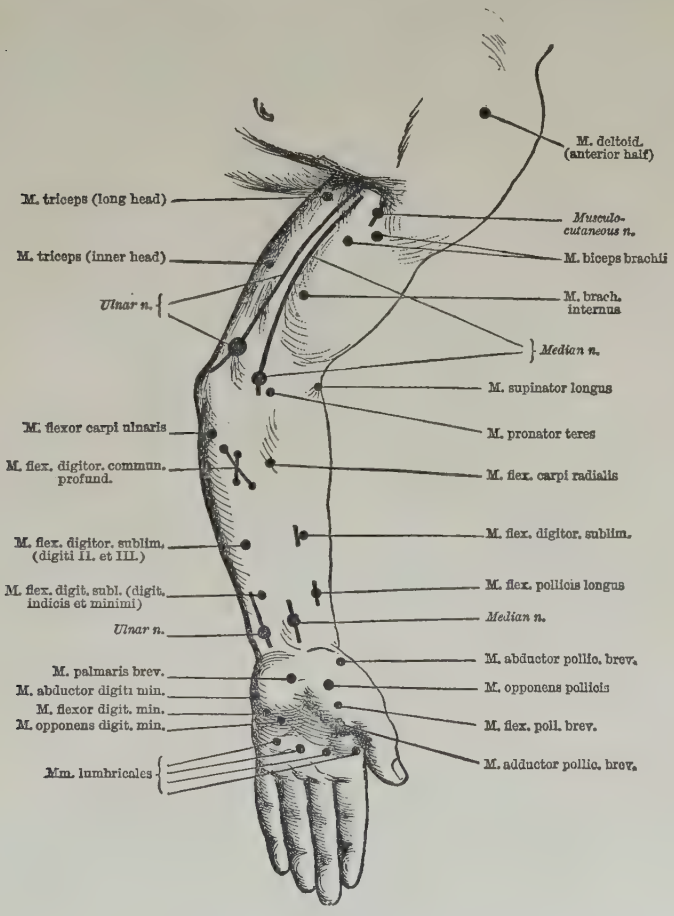

FIG. 28. — The Motor points. The Flexor Aspect of the Upper Limb.

or decreased accordingly; the irritability to induction coil currents (faradic irritability) being abolished both in the nerve and the muscle. This condition is known as the *reaction of degeneration*, and is found in cases of serious injury or disease in the motor nuclei of the anterior cornua, or in the nerve trunks.

The importance of the reaction of degeneration lies in the valuable help afforded by it for localising the seat of disease.

Other modifications of the normal reactions are a *general increase of irritability to coil and battery, a corresponding general decrease of irritability, and a partial reaction of degeneration,* whose essential features are the presence of sluggish contractions when the muscle is stimulated directly by a battery current, and a partial retention of the excitability of the nerve and muscles to the induction coil current. This partial reaction of degeneration most usually occurs as a transient phase in a paralysis which is becoming either worse or better; and it may be seen in other cases where the damage is not sufficient to produce a complete reaction of degeneration.

Practical Electrical Testing. — This should be carried out as follows:

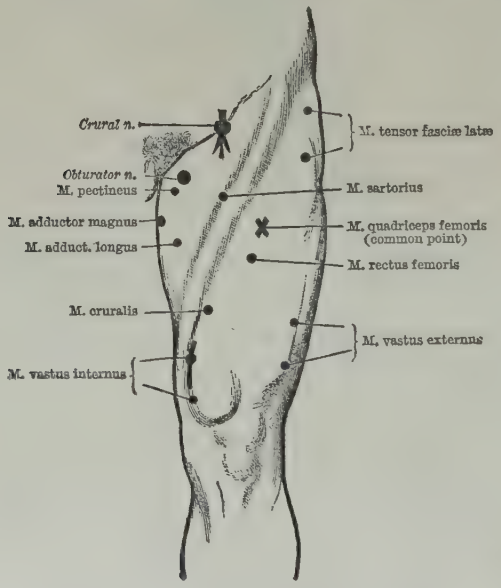

FIG. 29. — The Motor points. The Front of the Thigh.

Place the indifferent electrode in a suitable position on the patient, and take the limb to be tested in the left hand, holding in the right the testing electrode with one inch disc which should have a key in the handle for closing the circuit. Moisten the skin thoroughly over the muscles to be tested, and set the induction coil in action at a weak strength; then apply the testing electrode to the hand which holds the patient's limb, in order to estimate the strength of current. This should invariably be done before the electrode is allowed to touch the patient, as the protection afforded to him by this procedure is obviously very great. When thus the strength of the current is found suitable, apply the electrode to the motor points of the muscles in order, noting whether they contract. A finger placed lightly upon the tendons will often help

us to decide whether they contract or not, and will obviate the use of very strong currents. The limb should also be disposed in such a way as to exhibit the action of the contracting muscles. If the opposite limb be sound a comparison should be made of the two sides in order to discover whether there be any changes in the contractility to the induction coil. A rough comparison can be made by the help of the graduated slide of the induction coil or by a suitable galvanometer, if such a one be at hand.

If the muscles all react satisfactorily to the coil test the case cannot

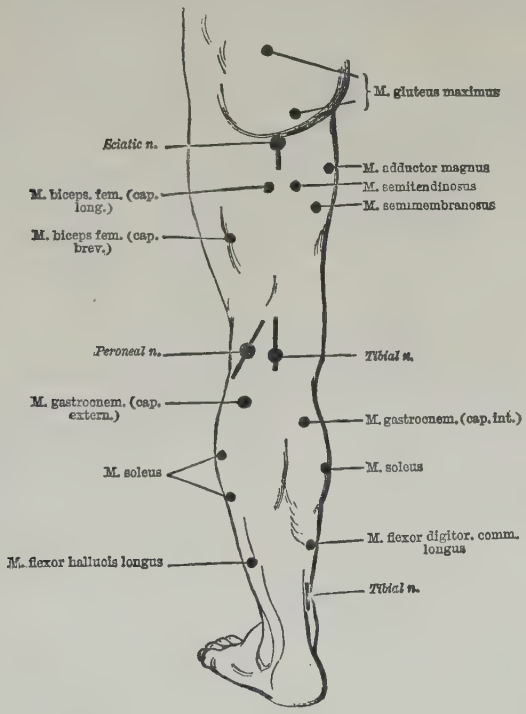

FIG. 80. — The Motor points. The Posterior Aspect of the Lower Limb.

be one of the complete reaction of degeneration. This should always be confirmed by going over them again with the battery current, noting whether the contraction is quick or sluggish, whether the anodal or kathodal closure is the more effective; and noting also the current in milliampères required to produce contractions. If the electrode be ever so little off the motor point the minimal contraction will require a stronger current than when it is rightly placed. Tables of *motor points* are given in most books upon medical electricity, but the best way to learn them is by careful practice upon one's own muscles. The nerve trunks of the limb should also be tried with both forms of current, and

their responses should tally with those obtained from the muscles themselves.

A knowledge of the positions and actions of the muscles, and of their nerve-supply, is quickly gained by the practice of electrical testing; and from the data obtained valuable opinions as to the seat and extent of the injury or disease can be formed.

Sensibility can also be tested electrically; the coil is to be used and the electrode applied to the surfaces of the skin, noting the position of the secondary coil at which a sensation is first felt. If the active electrode be applied to the operator, and the fingers of his own hand be

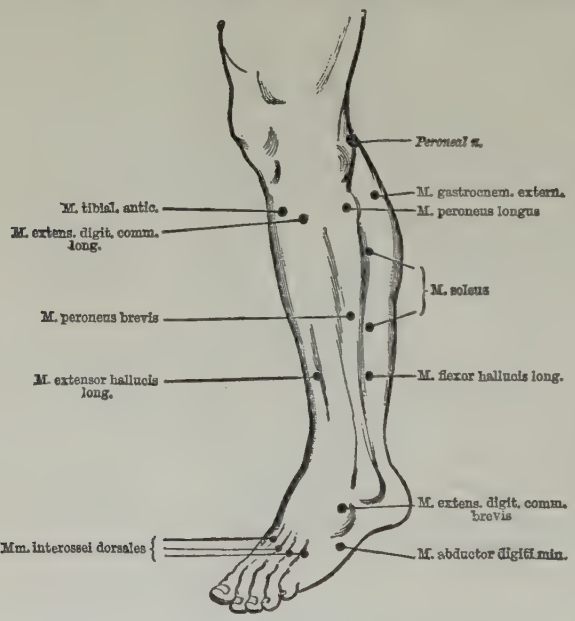

Fig. 31. — The Motor points. The Leg and Foot, outer side.

used as the electrode to convey the current to the patient, the sensibility of the patient's skin can be directly estimated; in this way the presence or absence of anæsthesia can be gauged with great nicety. In cases where tactile and common sensation are unequally affected, the electrical test determines analgesia rather than anæsthesia. Thus a patient with analgesia may be able to feel the touch of the electrode, though unconscious of the strong current which it is conveying into the skin.

Electrical Treatment. — This may be locally applied for the sake of influencing a particular part, or it may be applied generally. The application of localised electrification to cases of nervous disease has had the effect of diverting attention from the treatment of general morbid conditions by general electrification; but the value of the latter treatment is

now becoming more fully recognised. General electrification is very useful as a stimulating method of treatment in states of malnutrition or debility; for example, during convalescence after exhausting illness, in rickety children, in anæmic people, in the earlier stages of rheumatoid arthritis, and in some other conditions, such as general neuritis and neurasthenia. The best mode by far of obtaining the effects of general electrification is through the medium of the *electric bath*. For this an earthenware or wooden bath-tub is to be used, which is fitted with large metal electrodes at the head and foot. The patient is put into the bath with the water at a temperature of 99°, and the current is passed through it. The water carries off a large part of the current, but the patient's body is traversed by about one-eighth part of the total.

The induction coil current is the most effective, and the most generally useful in the electric bath. The patients make good progress under this mode of treatment and gain in weight; a large number of patients receive electric baths every year at the electrical department in St. Bartholomew's Hospital, and the value of the treatment is undoubted. Rheumatoid arthritis, if not too far advanced, is relieved. The use of a small bath as a means of carrying out electrical treatment for children is very convenient; it is well borne by them, and they like it; the action of the current is also more uniform and thorough than when treatment with the ordinary moistened electrode is used. The electric bath may also be used as a means of applying local treatment if the parts involved be of considerable extent; by so doing the risk of chill is diminished, and the currents affect the cutaneous nerves less painfully because of the good moistening of the skin. Thus children with infantile paralysis of the lower limbs improve more quickly when their treatment is applied through the medium of a small warm bath; and if one leg only be affected, the sound leg can be drawn up, and the current diverted into the paralysed limb. I have been extremely pleased with the results obtained in this way. The electric bath unfortunately has suffered much in repute from the abuses connected with it; but there is no doubt whatever that, when properly applied, it is a most valuable means, and its uses will in time be more fully recognised. The deplorable quackery which has degraded medical electricity of late years has had the effect of destroying the confidence of the medical profession in the treatment; but this attitude tends to perpetuate the evil, which should rather be dealt with by medical men themselves taking up the study and practice of medical electricity, and withdrawing their support entirely from all unqualified "medical electricians," who are uniformly to be regarded with suspicion. It may be assumed that all such persons are likely sooner or later to abuse the confidence placed in them, and to yield to the temptations of treating patients on their own account, either by selling them "electric" or "magnetic appliances," or by promising impossible cures.

General electrification by means of an electro-static machine has already been referred to. It has the advantage that it does not require

the patient to undress, and it appears to be of some value in certain cases; the use of electro-static treatment for cutaneous affections, and especially for pruritus and for chronic varicose ulcers, deserves a trial, as it has been found to be of great value by certain French observers. The methods of application will be found in the special handbooks.

Localised electrification for local affections has been tried in a vast number of diseases; indeed there are few morbid conditions for which electricity has not at one time or another been recommended. The modes of application are simple. The indifferent electrode is applied to the body in such a way that the path of the current from it to the active electrode shall follow as closely as possible the line of the nerves of the part to be treated. An active electrode of suitable size and shape is then moved over the affected region (labile application), or held firmly over one part (stabile method), the skin and the electrode being well moistened; ten minutes is a suitable length of time. The treatment should be repeated two or three times a week, the choice of current — whether of induction coil or of constant current — will depend upon the effects desired; for the stimulating and trophic effects which form so large a part of ordinary electrical treatment the induction coil is the best as a rule.

The properties of the current can be represented by the accompanying table: —

Effects desired.	
A. Stimulating and trophic	(1) Induction coil. (2) Battery current with variations, interruptions, and reversals.
B. Anodyne.	Battery current. Positive pole without interruptions or sudden variations.
C. Electrolytic D. Alterative and vasomotor	Battery current, without reversals. C. Peripolar effect. D. Interpolar effect.
E. Osmotic	Battery current. Positive pole.

The striking effect of electrical currents in causing contractions in paralysed muscles has naturally attracted attention from the first as a possible therapeutic method. In certain kinds of paralysis electricity affords a very useful means of treatment. In *Hemiplegia* from organic disease it cannot indeed be expected to restore parts which have been destroyed; but a short course of treatment during the period of recovery does help materially in the restoration of power to those which are not too severely damaged. It appears that the paralysis which follows a hemiplegic attack is often more extensive than is warranted by the actual destruction of fibres in the brain, and the electrical treatment favours the return of functional activity in those parts which have been disused, or impaired though not destroyed by the cerebral lesion. I have seen few cases of hemiplegia which have not gained something from a month's treatment by electricity. The application of a fairly strong induction coil current to the affected limbs, so as to produce lively con-

tractions of the muscles, is the proper method; it should be done twice or thrice a week for ten minutes at a time, and this treatment carried out for a month. By the end of that time the patient will have derived whatever benefit he is likely to obtain. It is important not to begin electrical treatment until from four to six weeks after a seizure.

Infantile Paralysis. — In this disease electrical treatment is of great value, but demands much perseverance on the part of all concerned. After the close of the febrile attack which usually accompanies the onset of the disease, the damaged muscles rapidly waste to a greater or less degree, and the reaction of degeneration may be well marked in some of the muscles within a week of the onset. At the end of three weeks the muscles may be tested, and the extent of the damage estimated; electrical treatment should then be begun. It is customary to use the induction coil if the muscles react to it; if they do not, to use the battery current instead: in either case the active electrode is moved over the surface of the paralysed parts. It is at present by far too common a practice to leave cases of infantile paralysis to themselves, in the belief that the muscles will recover spontaneously if the motor cells in the cord are not destroyed; or will remain incurably atrophied if these cells are destroyed. This, however, by no means represents the true state of the case. From a fairly wide experience of electrical testing and treatment in infantile paralysis, I may definitely assert that there are many cases of children in which weak and damaged muscles remain inefficient during years of such "expectant treatment," although they present no reaction of degeneration. These are cases which will at once begin to improve with electricity, and will continue to improve if the electrical treatment be continued. There are also many cases where muscles, atrophied and degenerated for two or three years, and giving no response to any form of electrical stimulation, may be made to grow and recover normal reactions by patient electrical treatment. The secret is that infantile paralysis does not of necessity destroy the whole of an affected muscle; this is the exception rather than the rule. A few normal fibres and a few of their ganglion cells very often survive, and by the persevering treatment of these a new muscle can be slowly cultivated. Thus in one case a new and useful calf gradually grew where there had been complete atrophy, the new muscle consisting almost wholly of a highly-developed outer head of the gastrocnemius; the inner head of the same muscle and the soleus remained atrophied. If, by treatment, a certain degree of development can be gained, so as to enable the muscle to be of service, then the voluntary use of it continues the process of repair. Exercises are therefore an important adjunct to the electrical treatment.

In brief, the treatment of infantile paralysis is most encouraging, and should by no means be neglected in children. No case should be regarded as hopeless, for however bad it may be, some gain from a course of treatment is certain; the gain may be but trifling, or it may be great, but there is no better treatment; and the parents should be

encouraged to continue it for years if necessary. I have had several cases under treatment for three years or more. When the disease is of several years' standing the prospects are less favourable, but even these will make some progress under careful treatment. The method of treatment to be followed may be with one electrode applied to the nape of the neck in the case of paralysis of an upper limb, or to the dorsal or lumbar region for the lower; the active electrode is to be moved over the affected muscles for ten minutes three times a week or oftener. The induction coil is to be used for all the cases; and for those showing altered reactions the constant current also, five minutes with each. The strength of current must be regulated by the feelings of the patient, some children being more timid than others; but as a general rule the current should be as strong as they are able to bear without discomfort or distress. The skin should be well soaked in hot water to diminish its resistance. Two-inch electrodes should be used and kept in movement over the affected muscles all the time. In this way children may bear the passage of three, four or five milliampères; but if not, then smaller currents must suffice. Although the constant current has the reputation of being the best for these cases, the grounds for its preference are more theoretical than real, and an induction coil apparatus will give good results. When the parents or the nurse are to carry out the treatment for a year or more the coil is the best apparatus, as it is simpler and cheaper, and any failure in its action is easier to detect by the cessation of the audible vibration of the contact-breaker. There is also no risk of damaging the patient's skin by electrolytic action.

The best way of treating these cases when the paralysis affects the lower limbs, as it so commonly does, is to arrange two metallic plate electrodes at the ends of an ordinary foot-bath of wood or earthenware filled with warm water. The child can be put into the bath in a sitting posture with legs extended, and the coil current passed through the bath; the strength of the current can be gauged by putting the hands into the water, one close by each of the electrodes. The bath can be given daily in the evening; after it the limbs are to be well rubbed, and the child put to bed. A little warm jacket can easily be contrived to cover the arms and trunk during the bath. Rubbing and manipulation of the affected limb, with some suitable gymnastic exercises, are of great advantage as auxiliaries in the treatment of this disease. The only way of ensuring proper treatment for these children is to entrust it to the mother or to a good nurse, to teach them carefully how to do it, and to have it done every day. It is useless to leave it to the visits of a medical man. The treatment must be made a part of the child's daily life; but the medical man must see it done now and then, and must test and measure the limbs from time to time to estimate the progress of the case. For this reason a simple apparatus is essential, and such an one has been contrived by myself for the express purpose of enabling the parents to manage the daily treatment for themselves without the possibility of going wrong.

Injuries of Nerves.— The different forms of paralysis, due to contusion,

compression, or other injury of nerve-trunks, improve rapidly under treatment if the nerve-trunk be not actually divided or torn across. When this is the case, an operation to unite the ends must be performed before electricity can be of service. When a nerve-trunk is involved in scar tissue the cases are likely to be tedious; but even here perseverance with the treatment will do much. There are few forms of paralysis more likely to improve under electrical treatment than those of damaged nerve-trunks, but the prognosis should be a guarded one until the actual severity of the injury can be gauged. If the electrical reactions be not altered, and if the reactions to the induction coil be present, the case may be expected to recover within four weeks; often it will get well in a shorter time. In neglected cases electricity will often start an immediate improvement. The exciting cause of the mischief, if still present, must be removed; this applies, of course, chiefly to crutch palsy. When there is a marked reaction of degeneration the case may be a longer one; the progress of the case during the early days of treatment must be watched, and the prognosis based on the state of atrophy and the amount of voluntary power and sensation present. Often it happens that improved nutrition and voluntary power begin to return before any change in the electrical reactions can be detected; in fact, this is the rule. In every case perseverance with the electricity, aided by rubbing and shampooing, is to be insisted on; in electrical treatment of these cases one need never despair except when the wasting and paralysis grow worse in spite of all that is being done: in such cases the nerve-trunk has probably been torn, and a surgical operation, to explore and, if necessary, to reunite the nerve, should be considered. When the reaction of degeneration becomes more and more difficult to elicit, requiring stronger currents than it did before, the prospects are unfavourable. The site of the lesion in the nerve-trunk can be localised very closely by electrical testing and examination of the affected muscles. The commonest types of paralysis from injury to nerves are sleep palsy, crutch palsy (musculospiral nerve), paralysis from blows about the shoulder (circumflex nerve, supra-scapular nerve, and nerve to serratus magnus), and median or ulnar paralysis from fractures and wounds of arm and forearm or from tight bandaging or badly-applied splints. These last two causes are not very uncommon, and they should be borne in mind. In the lower limb paralysis from injuries to the nerve-trunks is less frequently seen.

Facial Palsy. — Facial paralysis in most cases also belongs to the same group: its symptoms need not be described here. It is important to remember that the electrical examination of the muscles of the face must be carried out with very weak currents; the skin is very sensitive, and as the muscles lie close beneath the surface they are readily thrown into contraction. Care must therefore be taken not to alarm the patient by the use of strong currents on the first visit. If the electrical reactions be normal the prognosis is good, and the patient may be expected to recover in from three to four weeks. If there be a reaction of degeneration, partial or complete, a longer time must be allowed. As a rule,

cases of facial paralysis recover unless some progressive disease in the course of the nerve be the cause of it. The cases which come on spontaneously and are usually ascribed to cold may be expected to recover. Too confident a prognosis must not be given, as now and then an apparently simple case resists treatment obstinately. Cases of long standing and those in elderly people are as a rule less favourable; but treatment must be persevered with, as improvement may begin to show itself as late as three months after the onset.

Electrical treatment will often start improvement in cases which are stationary; and it is desirable to begin electrical treatment early, and not to neglect it until a late stage of the complaint. Many cases of facial palsy recover without electrical treatment; but it is not wise to leave the cases untreated. The induction coil is best for those with normal reactions; if the reaction of degeneration be present, it should be supplemented by the constant current, negative pole. The indifferent electrode should be applied to the back of the neck, and the active electrode moved over the face, following approximately the lines of the main branches of the facial nerve. The skin must be very thoroughly moistened to diminish the unpleasantness of the current. The electrode should be kept away from the points of emergence of the main branches of the fifth nerve, as these are very sensitive.

Neuritis. — In the various forms of paralysis due to general or multiple neuritis, the best treatment by far is by the electric bath; the induction coil and fairly strong currents are to be used, and the same treatment should be adopted in paralysis following specific fevers, of which diphtheritic paralysis is the type. Failing the electric bath, the induction coil may be used with large sponge electrodes. The patient must be guarded from the risks of chill by using hot water and a well-warmed room, and it is often most convenient to apply the treatment at bedtime, as the patients will probably sleep all the better after the electrical treatment. The electric bath is much more agreeable and efficient than the treatment by sponge electrodes. Cases of advanced alcoholic neuritis sometimes recover completely under prolonged bath treatment. If the interrupted current cause painful sensations the constant current may be used instead.

Lead Poisoning. — The treatment of lead poisoning is slow: in hospital patients it is usually made slower because the patients return to their work as soon as they begin to recover power, and then they again come into contact with the sources of lead poisoning.

In this disease one may occasionally notice that muscles give a reaction of degeneration even before they are affected with paralysis; and, conversely, the atrophy and paralysis may improve considerably before there is any return of the normal reactions.

The electric bath with constant current has been proposed in cases of metallic poisoning as a means of eliminating the metal from the system. I have found unmistakable traces of lead deposited upon the copper electrodes of the bath from a patient with lead poisoning. It is doubtful,

however, whether the lead so deposited has been obtained from the tissues of the body, or whether it comes from the contamination of the surface of the skin with lead compounds. Further experiments are necessary before the point can be cleared up. The battery current, labile over the affected muscles, is the treatment most favoured. It should be combined with induction coil treatment, each current being applied for five minutes at each visit.

Neuralgia. — Neuralgia sometimes yields quickly to electricity, at other times it is most obstinate. Often the pain is made worse by the induction coil, but by using a secondary coil of many windings and a rapidly vibrating contact-breaker, an anæsthetic effect can be obtained which has proved to be decidedly useful in many cases. In general the an-electrotonic effect of the positive pole of a constant current battery should be tried; there must be no abrupt makes and breaks of current, and the strength must be raised and lowered very gradually by the use of an adjustable resistance of about 10,000 ohms. With this in circuit, and set for its maximum resistance, the current collector is slowly turned on to twenty cells, the contact of the electrode with the patient being steadily maintained; the current is then increased by sliding the traveller of the rheostat from its maximum to a lower value, until five or six milliampères are indicated on the galvanometer. The electrode is kept moving slowly over the neuralgic area, but without any interruptions of contact until the end of the sitting, then the rheostat is again brought into use to lower the current, and afterwards the current collector is turned off. Five minutes is a sufficient time for each sitting.

Sciatica is a painful affection which commonly comes under electrical treatment; the results are usually good, and may be manifested rapidly. As the nerve is deep-seated, large electrodes and currents of ten to twenty milliampères are to be employed. The indifferent electrode (negative pole) is to be placed on the sacrum or over the sciatic notch, while the other pole is moved slowly along the trunk of the nerve, and also applied to any painful points which may be present. The electric bath is also a valuable method of treating sciatica: one electrode may be placed near the posterior surface of the thigh, while the other is at the head of the bath; or the electrodes at the head and foot of the bath may be used, and an accessory wire led from the foot-plate to a pad electrode placed under the thigh; this electrode must be covered with a flannel or wash-leather covering. The painful counter-irritation of a strong induction coil current, applied with a wire brush to the dry surface of the skin of the affected region, will sometimes dispel a sciatica.

The treatment of *Lumbago* is similar in all respects to the treatment of *Sciatica*, except that the electrodes are to be applied to the lumbar, and not to the sciatic region. The results of electrical treatment for sciatica and lumbago are very satisfactory.

Hysterical affections may often be dispelled by electrical treatment, and many of the remarkable cures to be found in the early books on the application of electricity to medicine are of this sort. This use of

electricity is none the less valuable in medical treatment because its effects may be due to an action upon the mind of the patient, for in hysteria some such profound mental impression, acting through the sensory nerves or otherwise, is chiefly required; but the cures effected by its means can only be attributed in an indirect way to the electrical properties of the apparatus employed. Occasionally the mere sight of the electrical apparatus is sufficient to dispel hysterical symptoms.

Electrical treatment, though it may cure the particular symptoms which are present at the time, does not alter the peculiar hysterical tendencies of the patient. In anæsthesia, contractures, paralysis, painful joints, weak spines, aphonia, etc., local stimulation with the induction coil, either with the ordinary electrodes or with the wire brush, are to be used. The symptom often departs suddenly during the course of the first sitting, or it may gradually disappear afterwards. It is seldom that more than a few repetitions of treatment are needed, and meanwhile other treatment to improve the patient's general state of health should be adopted. The electro-static machine is also a very useful engine for the treatment of hysterical manifestations.

Neurasthenia and Hypochondriasis. — Patients suffering from these maladies are usually very ready to try electrical treatment, partly from the general tendency of such patients to seek remedial measures of any kind. From electricity, as from any other new thing, they seem to derive benefit for a time. Perhaps the best thing for them is to apply general electrification, particularly the electric bath with interrupted current. The general fillip to the system afforded by this may help to raise them out of their unhappy condition, especially if combined with a diet and regimen calculated to improve their digestive functions. In many of these cases the symptoms are associated with disorder of the alimentary canal, such as dyspepsia or constipation; and it may be that improper diet and malnutrition are the immediate cause of most cases of hypochondriasis and neurasthenia. Electricity can help them by stimulating their metabolic processes, and so can indirectly provide them with a chance of escape from their miserable condition, provided that in other respects their diet and mode of life can be improved.

Insomnia. — It has often been observed that patients sleep better after electrical treatment, electricity is therefore a proper means to try in cases of sleeplessness. General treatment with the induction coil, either in the electric bath or by means of large bath sponge electrodes moved over the trunk and limbs, will thus enable many patients to sleep soundly.

The treatment of *locomotor ataxy* and *progressive muscular atrophy* by electricity has been hitherto very unpromising, although the pains of tabes have been alleviated by the treatment. Favourable reports are published from time to time of cases of these diseases improved by electricity, but no thoroughly definite results of an uniform character are yet to hand.

The troublesome symptom of *tinnitus aurium* may often be relieved,

but rarely cured by electrical treatment. The tinnitus is sometimes associated with increased electrical irritability of the auditory nerve, and it can be diminished if the anode is applied to the ears by means of a divided electrode shaped like the metal part of a binaural stethoscope, the indifferent electrode being placed on the nape. To protect the skin from electrolytic effects, there should be a thick covering of wetted absorbent wool upon the active electrode, which is to be applied just in front of the tragus. A current of ten milliampères is to be used for ten minutes. It may be turned on rapidly, but should be turned off very slowly, and with the help of an adjustable resistance. In favourable cases the tinnitus is arrested during the passage of the current, and after a few sittings the remissions become longer and longer until the symptom disappears altogether. When patients with tinnitus come for electrical treatment, they should be submitted to an electrical testing. If the anode modify or arrest the sounds, the cases are favourable, and electrical treatment may be confidently recommended. If the current leave the sounds unaffected the cases are unfavourable. The kathode usually increases the sounds, the anode diminishes them. Sometimes the converse is the case, then the kathode must be used as the active electrode. If the sounds are unaffected by either kathode or anode, treatment is not likely to be of much use.

Disorders of Circulation. — Dr. Barlow has recommended electricity in those cases of local asphyxia, known as Raynaud's disease, in which the extremities become blue and cold, and are liable to chilblains, or even to gangrene. The mode of treatment is as follows: The hand or foot is immersed in a basin of warm water in which one pole of the battery is placed, while the other is fixed to the upper portion of the limb, or to some neighbouring part of the trunk; the current should be as strong as the patient can bear. Dr. Barlow advises the use of the continuous current, but probably the interrupted current would prove equally efficacious. The same treatment is very good for patients who are subject to chilblains, and will prevent their formation, or dispel them, if the treatment be begun as soon as the first signs of the chilblains show themselves. If the skin be broken it is difficult to apply electrical treatment, as it produces a good deal of pain in the excoriated surfaces.

A course of electric baths usually cures any acne of the skin of the back that the patients may suffer from, and I have seen a chronic eczematous ulcer of the leg, after having been a great trouble for years, resisting many remedies, heal in a few weeks under the use of the induction coil bath.

Exophthalmic Goitre. — The electrical treatment of this disease has received a good deal of attention, and from time to time favourable results have been obtained and published. Among the most recent publications on the subject is an account by Dr. Rockwell of forty-five cases; the method which he recommends is to use strong electrical currents — twenty, forty, or even sixty milliampères. These are applied by means of electrodes of very large surface; the kathode over the pit of the

stomach, and the anode to the nape of the neck. General electrical treatment by the electrical bath, or otherwise, may be used concurrently. Vigouroux has recommended the use of the induction coil, applying it in turn to the eyeballs, the chest, the thyroid, the sides of the neck, and the cardiac region. Other writers advise other operative procedures; there is no certainty of relieving the patient by any of them. Electrolysis of the enlarged gland is perhaps the most promising method.

Incontinence of urine is also a favourable subject for electrical treatment. In the reflex *nocturnal* incontinence of the young it is usually successful. One electrode is applied to the lower dorsal spine, and the other to the perinæum, and the induction coil current is used for six minutes, followed by the battery current for three minutes. The latter current should be repeatedly made and broken and reversed by hand; about fifty such interruptions will suffice. Current five to ten milliampères, positive pole to spine, negative to perinæum. Improvement soon shows itself, but treatment must be continued for a month, or several months, as the cases are very apt to relapse. The effect of electricity here is to stimulate the centres, both cerebral and spinal, by the repeated setting up of painful local impressions, which in time bring the inhibitory cerebral mechanism into closer relation with the reflex centres in the lumbar cord. Usually the patients begin by being free for a night or two after each application, and they go on gradually improving. It may take some time to overthrow completely the bad effects of habit in these cases, but with perseverance they will all improve, if there be no organic mischief behind. It is important to try to combat the tendency to very deep sleep which many of these patients exhibit. This may be done by various means — for example, the bedclothes should be scanty, and a clock which strikes the hours loudly may be placed in the bedroom. When the incontinence is *diurnal*, and due to weakness of the sphincter, the best mode of application is the introduction of a metal-tipped sound into the urethra, the indifferent electrode being as before; the same treatment with the induction coil followed by galvanism should be employed. This state sometimes follows when patients have been forced to hold their water for a long time. In women a small want of tone in the sphincter is not at all uncommon, and the urine is apt to be expelled involuntarily during any muscular effort. I have seen electrical treatment cure a number of such cases permanently, even when one hardly dared to hope for so fortunate a result. When the bladder symptoms form part of a general paraplegic state, the local treatment described above will not be of use unless the condition of affairs in the spinal cord can be improved also.

Electricity has been applied for various uterine affections, particularly for uterine fibroma. The methods of Apostoli have fallen into discredit in this country, but no doubt there is some value in his treatment; in Paris he continues to carry it out, and is able to publish favourable results in large numbers of cases: moreover, independent

observers have confirmed his statements. It is quite possible that it may again be revived here.

The use of electricity for surgical purposes — for the heating of wires in the galvano-cautery; for the lighting of small incandescent lamp instruments; for the destruction of nævi, moles and warts, and the removal of superfluous hairs, are fully dealt with in the special articles and handbooks.

H. Lewis Jones.

Among the standard works on the medical uses of electricity the following may be enumerated: —

1. Boudet de Pâris. *Électricité Médicale*, 1888. — 2. Dawson Turner. *Medical Electricity*. Ballière, Tindall and Son, 1892. — 3. Duchenne. *Électrisation Localisée*, 1872. — 4. Duchenne. *Électrisation Localisée*, translated in part by Dr. G. V. Poore. New Sydenham Society, 1883. — 5. Erb. "Electro-therapeutics," in von Ziemssen's *Handbook of General Therapeutics*, vol. vi., translated by De Watteville. Smith, Elder and Co. 1887. — 6. Hedley. *Hydro-electric Methods in Medicine*, 1892. — 7. Lewis Jones. *Medical Electricity*. H. K. Lewis, 1895. — 8. Onimus and Legros. *Traité d'Électricité Médicale*, 1888. — 9. Steavenson. *Electrolysis in Surgery*. Churchill, 1890.

H. L. J.

MASSAGE: TECHNIQUE, PHYSIOLOGY, AND THERAPEUTIC INDICATIONS

No endeavour will be made in the present article to consider the history of massage, but to give simply and briefly an outline of the technique sufficient to enable a physician to judge whether a masseur is well taught and works conscientiously; then to recapitulate the physiological effects which experimental studies have of late firmly established, to deduce from these its applicability in disease, and to indicate the diseases in which clinical experience has taught us its usefulness.

No doubt some of the distrust of massage has been due to the ignorance or incompetency of many of the professional manipulators, and to the absurd and extravagant efforts to proclaim it as an exclusive method of treatment. Unless inflammation be present, or some unusual tenderness or susceptibility, little direct harm, beyond discomfort, is likely to be done to a patient by rough or wrongly applied massage, but failure of any good result is harm enough. The practice of "mechano-therapy" by manipulators usually quite ignorant of medicine, certainly with no scientific training, and independent of proper diagnosis and directions from a physician, is altogether to be deprecated, and is one of the great sources of the prejudice against the method still existing in the minds of many medical men. It is not necessary that such work should be undertaken by the practitioner himself — though this has been done in Germany and Sweden — but that he should be sure, if need be by per-

sonal observation, that the person he employs is well taught, industrious, conscientious, and obedient to orders.

The *technique of massage* is not difficult to acquire; and, as the whole value of the treatment lies in the proper execution of minute details, one who prescribes it should be familiar at least with the movements commonly used. "The various manipulations and their modifications naturally suggest themselves to one who clearly comprehends the anatomical, physiological, and pathological indications in any given case" (1).

With the single exception of Dr. Granville's percussor, no instrument, among the hundreds devised for the performance of some of the movements, can usefully replace the human hand. Great manual strength is not necessary, though a hand not too small is desirable; but very large and muscular hands lack the delicacy of touch which is so desirable. The most rational classification of the various movements is that into four kinds, for which the French names are usually employed, as follow: *Effleurage* (stroking), *pétrissage* (kneading), *friction* (rubbing), *tapotement* (percussion or striking). These may all of them be used lightly or strongly, deeply or superficially, and in various combinations, as needful for special ends.

Effleurage is performed with slow strokes, made with the flat or with the heel of the hand, or with its ulnar edge or with a finger only. The stroking should always be centripetal, the hand in the return movement only lightly grazing the skin. The chief usefulness of effleurage, apart from its slight stimulation of the skin-nerves, is in hastening the movement of the contents of the veins and lymphatics.

Pétrissage — the most important and most difficult of the several movements — is done by grasping with the whole hand the tissues to be manipulated, lifting them somewhat, and kneading them with an alternate tightening and loosening of the hold. In large masses of muscle, like those of the thigh or calf, it is sometimes best to use both hands. The movement is very different from pinching. Care must be used that the skin moves with the hand over the underlying tissues. The surface hairs will be painfully dragged if the hand is permitted to slip over the skin. In certain favourable situations — in the upper arm, for example — the extended hands are placed upon opposite sides of the limb and moved rapidly back and forth with firm pressure, rolling the muscle masses between them and pressing them together or against the bone, — a motion entitled "*fulling*," from its likeness to the movements used by fullers in handling linen. The effects are identical with those of ordinary pétrissage, but somewhat more stimulating from the greater speed of the manipulation. A slight contraction of the muscles is induced by this operation, the absorption of infiltrations in the tissues is promoted, and their progress through the lymph-vessels assisted.

Friction is performed by firm rubbing in small circles with the thumb, finger-tips, or whole hand. It might well be included as a modified form of pétrissage, as it has precisely similar effects, and is useful where the tissues are too closely attached to bones to be picked up by the hand, as

in the neighbourhood of joints; in such situations it is especially of value in the removal of articular effusions.

Tapotement is the application of rapid blows delivered with the ulnar edge of the hand, with the tips of the bent fingers, or with the flat of the open hand. The end to be attained and the tissue to be affected decide which method shall be used. It acts for the most part as a mechanical stimulant. If we wish to excite the peripheral skin-nerves we use the flat hand — for instance, in anæsthetic areas; to reach a nerve-trunk, blows with the finger-tips, rapidly delivered from the wrist (not using the whole forearm in a hammering fashion), are employed, and, to excite muscles, "chopping," with the edge of the hand, transversely to the long axis of the muscles.

The French and the Swedish masseurs have wasted much ingenuity in subdividing the several manipulations with great subtlety, and some operators perform a great variety of what can only be called ornamental movements, fantastic flourishes and airy graces, like the affectations of a fashionable pianist.

In the consideration of the force and frequency of application desirable in any particular case, the usual direction to the student of massage must be remembered, namely, that his mind is to be given not to the movements his hands are making, but to the tissues upon which he is operating and the effect he wishes to produce. The force, therefore, must be such as to attain the desired end, and this will necessarily vary with the state of the tissues and the condition of the patient. In a chronic arthritis with firm exudation vigorous friction will be required; in a more acute trouble — a sprain, for instance — much less force will be needed; at first, certainly, only light effleurage. Nervous, hysterical, or excitable patients must be very gently handled at first, and only for short periods. In certain cases (again a recent sprain may be cited as an example) massage three or four times daily will be of service, each application lasting only from five to fifteen minutes. Most massage procedures, to be of use, should be repeated at least once daily. General massage, such as is used for convalescent patients or "rest-cure" cases, must last from thirty minutes to an hour every day.

The usefulness of massage is greatly lessened by the common practice of employing some oily substance for lubricating the skin. Moreover it is dirty; and the excuses offered that, unless an oil be applied, the operator will pinch unpleasantly or will pull the hairs painfully, are confessions of incompetency. In old or much emaciated patients, whose skin is harsh, dry, and scaly, it is sometimes desirable to use an emollient; and for such purposes the best unguent is lanolin with the addition of enough oil of sweet almond to render it of the consistency of thick cream. Vaseline is difficult to remove satisfactorily after use, is not absorbed, and to some skins is irritating. Generally it may be said no oily application should be used without the physician's orders.

There can be no question of the much greater value to the patient of massage when used directly upon the skin. Done through clothing, even

the thinnest, the operator must fail in technique: the palpation of the tissue will be imperfect, and an additional amount of force must be used.

General massage is a form of passive exercise for those unable to take active exercise, or for whom active exercise is undesirable. It is usual, but not important, to begin with a lower extremity. After manipulating the foot the leg is worked with kneading, fulling, effleurage, and friction about the joints. It is best to put a sock or stocking on the foot when the massage is over; and every care must be taken to keep the parts warmly covered with a blanket as they are finished. After the legs the operator proceeds to the arms and treats them in the same way. In massage of the back vigorous, rapid effleurage over the spine is employed, as well as the treatment to the muscles. In rubbing the chest in women the breasts are usually left untouched. Last comes the very important operation of abdominal massage. In order to obtain relaxation of the abdominal muscles, the head is raised upon a pillow and the knees bent, while the patient is directed to breathe deeply. At first there is always difficulty in overcoming the tension, largely involuntary, of the recti abdominales, especially in hysterical women, but as they grow accustomed to the manipulation the muscles slacken. Deep friction in small circles, continued over the whole abdomen, is made first, using the fingers of one hand; kneading movements, chiefly with the heel and palm, in a large circle round the navel; then similar applications are made over the large intestine, beginning at the right iliac fossa, and following the course of the ascending, transverse, and descending colon; the hands are placed on the two sides below the ribs and drawn forward with deep pressure several times; the region of the liver and the left hypogastric and hypochondriac regions are kneaded, reaching in this way the small accessible portion of the stomach, and the whole process ends by the operator grasping the abdominal walls lightly, but firmly, and imparting a rapid vibratory movement to them and to the underlying structures. Occasionally tapotement or clapping with the hand over the liver may be added to these procedures. After the completion of the massage the patient should be warmly covered and lie quiet for an hour.

The effects of general massage are very decided and apparent. The immediate results are a fine sense of well-being, a feeling of comfortable tiredness without exhaustion, and a pleasant drowsiness. In rare cases hysterical patients are aroused and excited by it, and more rarely still, persons are found whom massage leaves chilled, irritated, and uncomfortable. In such cases the experiment may be tried of reversing in part the order of procedure, rubbing the abdomen first instead of last, then the chest and back, and finally the arms and legs. Occasionally it may be found that massage has been overdone, and that lighter applications are needed to give good results. Very seldom indeed do we find patients to whom massage is so disagreeable as to make its application entirely impossible.

The later effects are also well marked: the skin softens and shows a better colour; the appetite is improved as well as the digestion; the

bowels act more freely; sleep is more prolonged and sounder, and the muscles become larger and firmer. The results in cases of disease will be considered later in more detail.

Studies of the results of massage in health and in various maladies have been numerous and valuable in late years; the work of Bunge, Brown-Séquard, Ziemssen, Weir Mitchell, Playfair, Sinkler, Gerst, Goodhart, Kleen and Profanter, taking the subject from the clinical side, has been confirmed and wider possibilities for massage application suggested by the physiological experiments of several of these same observers, as well as by the labours of Lombard, Mosso, Maggiora, Lassar, Eccles, Glovetzky, Mosengeil, Mezger, Kronecker, Lauder Brunton and Tunnicliffe, Winternitz and Zabludowsky.

The *immediate effect of massage* is to increase the amount of blood in the region rubbed; the skin is flushed, the vessels in the muscles receive a larger amount of blood, and the flow of blood is greater through the part for some time subsequently. Accompanying this there is a fall of general blood pressure and a slowing of the pulse, if the manipulation has been a deep muscular stimulation. Superficial skin stimulation increases blood pressure. An increased activity in the movement of the lymph-stream has also been accurately demonstrated.

It is obvious that we have here a useful indication for *the treatment of recent local inflammatory conditions*, such as result from sprains, luxations, etc. The increased circulation will not only prevent stasis and the migration of white corpuscles into the tissues, but will rapidly remove the corpuscles and lymph which have been already thrown out. Again, the secondary effect of the larger amount of blood passing through the region is valuable in case of any local disturbances of nutrition, indolent ulcers, undue amount of deposit following fractures, contusions and myositis.

Donders, Pagenstecher, Damalix, Klein and others have reported successes in the treatment of both catarrhal and phlyctenular conjunctivitis, opacities of the cornea, pannus and even cataract, by means of massage. For full descriptions of their methods the articles by these and other ophthalmic surgeons must be consulted [*vide* References].

Besides these and such effects other general consequences are perceived. One result of the changes in blood pressure is an increased secretion of urine, another is that fatigue — whether local, as in an over-used group of muscles, or general — may be rapidly and pleasantly removed by massage, that is, by the removal of fatigue-products and by the flushing of the muscles and nerve-centres with quantities of fresh blood. Lombard, Mosso, Maggiora and Zabludowsky have shown by experiments in their own persons, or upon animals, the prompt power of massage to restore functional ability to exhausted muscles. Maggiora found that this improvement did not take place in muscles whose blood-supply had been shut off. He further concluded that tapotement and friction were less effectual than kneading, and this again not so useful as mixed massage; and that the beneficial effects of manipulation were, within

certain limits, directly proportional to its duration. That more blood actually flows through the tissues during and after the rubbing has been proved by the careful experiments of Lauder Brunton and Tunnicliffe. A series of clinical examinations of the blood before and after massage under very varied conditions of health and disease have recently been made by myself. Originally it was my intention to study the effects of massage in anæmia, but a wider field opened itself out as the very marked results in such cases appeared. In sixty observations upon thirty patients only three failed to show an increased number of red corpuscles after general massage. The conclusions reached were as follows: — In health massage increases the number of red corpuscles, and to a less degree and not so constantly, their hæmoglobin value. In all forms and grades of *anæmia* there is a very large and constant increase in the number of red corpuscles after massage; this is greatest about an hour after treatment, slowly decreasing from that time. This decrease is, however, postponed further and further if the manipulation be daily repeated. There is an occasional but inconstant increase in the hæmoglobin value, an increase proportionately less great than that of the cellular elements. The additional red corpuscles discovered by the Thoma-Zeiss hæmocytometer after an hour's massage was often as great as 20 per cent, and in some cases reached 50 per cent of the number originally observed.

The increased activity of the superficial circulation does not suffice to account for so great a change: moreover, if the increase arise merely from an addition to the number of red cells in the peripheral vessels at the expense of the rest of the circulating fluid, there should be an increase of hæmoglobin directly proportional to the increase in the red globules; yet in no case did the hæmoglobin-increment exceed 15 per cent, even when the cell-increase reached 50 per cent. It can scarcely be supposed that an hour's massage, much as it hurries the current in the vessels, can actually cause a greatly increased production of blood-cells; although the repetition of treatment no doubt stimulates cell-making. Still, the effect of this new activity and movement of the cells upon metabolic processes must, at any rate for the time, be much the same as if a considerable addition were made to their number. Further, these examinations make it seem in every way probable that, in health, there are vast numbers of corpuscles ready for use if called for, and also probable that a part of the trouble in anæmic diseases may be a lack of availability or of activity in the corpuscles, that many of them are sluggishly lingering in the by-ways of the circulation, and only forced or pushed into greater activity and usefulness by the direct stimulus of massage. "The state of things in the system in anæmias may be, to draw an analogy from economic conditions, like the want of circulating money during times of panic, when gold is hoarded and not made use of, and interference with commerce and manufactures results."

Effusions of lymph or blood in serous cavities, in the substance of muscles, and in the sheaths of the tendons or nerves, may be removed by

means of massage. Reibmayr and Höffinger injected water into the abdominal cavity of rabbits, subjected some of the animals to massage afterwards, and on opening the abdomens found that in those which had been massaged the proportion of the fluid absorbed in a given time was more than one-third greater than in those not so treated.

Von Mosengeil made injections of Indian ink into two joints in rabbits, and massaged one joint. Upon examining the articulation treated very little of the injected matter could be discovered in it, even when opened after only a few minutes' massage. The ink could be traced through the lymphatic vessels into the neighbouring glands. In the untouched joints the ink was found unchanged, no attempt at absorption having taken place.

Acute *arthritic disorders*, like rheumatism and gout, accompanied by general constitutional disturbance, are not suitable for massage until the acute stage has passed; but localised or traumatic arthritis and synovitis, where there is no risk of promoting the resorption of toxic products, may properly be so treated. The results in sprains, teno-synovitis and the like, are sometimes amazing; and, if massage be instituted immediately, speedy recovery may be confidently predicted. The sooner after the injury manipulation can be begun the better. At first the swollen, bruised, and tender structures should not be touched at all, but effleurage made from the seat of the accident centripetally, to hasten the circulation from the congested part and help to carry off the exudation. Similar stroking should be used below the injured part, and, before the end of the application (which should last ten to fifteen minutes), it will be found possible to give effleurage and light friction directly to the inflamed tissues. At first manipulations should be made several times daily, and a firm bandage put on in the intervals.

Where we find old synovial inflammation with thickened connective tissue and firmly organised deposits, much more force may advantageously be used; and such a case presents one of the few occasions where the use of some unguent is desirable, since sufficiently strong and frequently repeated friction will sometimes injure the skin unless a lubricant be applied.

Massage of the neck, in the form of downward stroking on the sides of the neck and friction and stroking from the occiput downwards, serves as a means of lessening the amount of the blood in the head by pushing onwards the venous flow. This manner of relieving cerebral congestion may be made use of for *insomnia*, where the activity of the brain is so great as to prevent rest, as it brings about that mild degree of cerebral anæmia which is the physiological condition necessary for sleep. Even where flushing, headache, sleeplessness, dizziness, and confusion of mind point to a threatening apoplexy, the same procedure is of service; and in migraine the effects are occasionally most happy. In the easily recognised complexus of symptoms somewhat loosely described under the vague name of "spinal irritation" — a state in which insomnia is frequently very persistent — effleurage, vigorously applied, will be found a

valuable aid in inducing sleep: here, however, it must be used upon the back as well as upon the neck. The technique is of the simplest. The operator, standing behind the sitting patient, lays the hands flatwise upon the lateral aspects of the neck below the ears, and pressing gently, strokes downward, over the jugular veins, at first with the ulnar edge of the hand, gradually turning the hand as it moves until the palm and then the radial edge carry on the movement. Pressure upon the hyoid bone and the larynx should be avoided.

Gerst has used the same means for the removal of the hyperæmia attendant upon concussion of the brain and upon fracture of the skull.

In *migraine, trigeminal and supra-orbital neuralgias, or neuritis*, much relief is felt from local massage; of course its use should not cause neglect of other measures, such as electricity, the regulation of the bowels and digestion, or remedies to combat the accompanying anæmia. In migraine especially it will be found necessary to continue the treatment for some weeks to be sure of benefit. In these affections it is very common to see the masseur work from the centre of the forehead toward the temporal region, a violation of the maxim, stated above, that movements should be in the direction of the venous currents. Manipulation should follow the course of the frontal vein, from the temples toward the root of the nose.

Sciatica, whether we consider it as neuralgic or neuritic, is much helped by carefully-applied effleurage. The German physicians prefer massage to any other treatment for this rebellious affection. Kleen's prescription is that as infiltrations (myositis in the glutæus maximus and medius muscles) frequently accompany or cause sciatica, careful palpation is to be made for these; and although, "on anatomical grounds, such infiltrations may readily escape the perception of the masseur, still the rule holds good . . . that energetic frictions should be made in this place, even if no pathological changes can be found. Furthermore, one should make vigorous tapotement with the fist along the course of the sciatic nerve as far as the hollow of the knee." Overstretching the nerve, by flexion of the thigh with a straight knee, pushed to the point of endurance, is, according to Kleen, to be added to the prescription.

Dr. Weir Mitchell has long abandoned these methods in obstinate sciaticas for a plan of his own which has been attended with remarkable success. To lessen the blood in the limb, and to remove the irritation caused by motion, the patient is confined to bed, the leg bandaged firmly from the toes to the groin with a flannel bandage, and the hip and knee joints fixed by a long splint from axilla to ankle, or, in patients who can be trusted to keep quiet, by sand-bags. The bandage is removed and the leg rubbed twice daily, general kneading of the muscles being used except of those near the nerve; even indirect pressure upon that structure is to be avoided. The nerve tract is to be "effleuréed" with long, steady strokes; the hip and knee joints passively flexed once or twice in a gentle manner, and the bandage reapplied. Three weeks of this procedure will usually suffice for a cure, even in obstinate cases.

Activity must be resumed gradually, and the use of the bandage and of a certain amount of rest in a recumbent position insisted upon for a time.

The treatment outlined for these neuralgias may serve to indicate the manner in which any form of neuritis or painful affection of a nerve may be handled by massage, whatever the origin of the disorder. The results of injuries, bruises, crushes, and even sections of nerves are relieved by the same applications, though of course the methods employed will vary somewhat with the character and seat of the injury, and the stage of the disease. Manipulations cannot be begun upon wounded surfaces until skin-healing is complete. The atrophy of muscles consequent upon nerve-section can be minimised, the period of disability much shortened, the subsequent contractions prevented, and the danger of pressure upon the nerve by scar-tissue lessened. In old cases of wounds of nerves where contractions, joint-stiffening, muscle-atrophy, and the various disturbances of sensation have all appeared from neglect of early treatment, massage is an indispensable instrument. It may perhaps be necessary to repeat what I have already urged, that such a statement must not be construed to imply the neglect of other aids — douches, faradisation of the atrophied muscles and of the muscles opposed to contracted groups, galvanism to the nerves, the forcible breaking up of joint-adhesions, etc.[1]

Contracted scars may advantageously be subjected to the same manipulations as contracted muscles, though, as such tissue is but ill-supplied with blood-vessels, the results are less striking. Firm pressure, squeezing, pinching, kneading, and, where possible, stretching are the methods employed. Of course, the earlier the case is seen, and the less firm the cicatrices, the more successful the result, as the further increase of scar-tissue may be prevented, and that already formed thinned and softened.

Writer's cramp and the allied forms of muscular difficulty, whether paralysis, tremor, or spasm from over-use of single groups of muscles, cannot be better combated than by massage and galvanism. The muscles usually affected are the flexors of the forearm or in the hand, and the occupations most commonly subject to the professional neuroses are writers, telegraphers, watchmakers, masons, or type-setters. The bicycle has of late given us a new form, in which the muscles of the thigh are affected; and one or two examples of an undescribed neurosis have recently been seen at the Infirmary for Nervous Diseases in Philadelphia in tram-car drivers, from the constant pushing upon the hand-brake. In all such disorders absolute rest of the affected part is the first requirement, and massage the next. Authors differ as to the proper technique, but probably the most effectual method is strong effleurage and pétrissage followed by tapotement to the affected muscles and to their nerves where these are accessible. In instances where muscular infiltrations

[1] For detailed cases of such disorders and their successful treatment by the means suggested the well-known work of Dr. S. Weir Mitchell on *Injuries of Nerves* may be consulted. The present writer has reported the later history of a number of Dr. Mitchell's cases in *Remote Consequences of Nerve Injuries and their Treatment.* Philad., 1895.

are found in connection with these palsies, or where neuritis is present, especial attention must be given to the parts thus affected.

Torticollis, when rheumatic in origin, yields readily to massage of the affected muscles. Where its cause lies more obscurely in an affection of the cervical portion of the cord massage is of less use, though it helps to relax the spasm, and may be of important service by strengthening the opposing muscles.

An excellent instance of the difficulty with which a new systematic treatment of disease makes its way is furnished by the facts concerning the application of massage in *chorea*. Blanche in 1854 presented to the Academie de Médecine in Paris a report of 108 cases of chorea successfully treated by massage, and for a time the method was fashionable, and has continued in use in France to a certain extent; but the majority of medical men continue to rely upon drugs, with a confidence unimpaired by the fact that no matter what or how much medicine be given the clonic movements continue for weeks. In the lesser degrees of chorea minor, arsenic, iron, fresh air, and proper feeding may be sufficient. In the more severe cases, even omitting the consideration of chorea major, bed, with massage, will be found to effect a very rapid and usually perfect cure. As the co-ordination improves, and the involuntary jerkings lessen, cautiously increased gymnastic movements should be added. Besides its influence over the muscles general massage is of value in counteracting the anæmic or chlorotic condition so commonly associated with the disease. Drs. Goodhart and Phillips in their series of cases of chorea treated by massage rather understate than overstate the favourable results.

In the treatment of many other disorders of the central nervous system massage has a recognised and well-established place. In *acute atrophic paralysis* it is at least helpful in maintaining nutrition. Dr. Gowers, Prof. Eulenberg, and others describe improvement in cases of *pseudo-hypertrophic paralysis* during its use. In the early stages of this disease it has certainly been my good fortune to see arrest of the progressing paralysis, and a decided increase in the strength of the weakened muscles.

In *locomotor ataxia* the effect is often astonishing, although one should remember that periods of rest, even of improvement, occur in this disorder without treatment. But the results exhibited appear too consistently in case after case to be the result of a fortuitous coincidence of the "normal" cessation of activity in the degenerative process with the beginning of treatment by massage. Patients with ataxia usually suffer less pains if they take little active exercise; and the mechanical treatment is useful in overcoming the ill-effects of this inactivity. Yet this alone would not account for all the improvements; the anæsthesia and paræsthesia disappear or lessen, as well as the lancinating pains; the insomnia, so often present, is bettered; even the difficulties of defæcation and micturition diminish. Recovery is not to be looked for — no power can renew sclerosed nerve-cells — but in a large majority of cases decided improvement may be confidently expected.

Persistent kneading, effleurage, and tapotement of the paralysed parts will do much to restore function in muscles palsied by *anterior poliomyelitis*, and massage and faradism should be continued in such cases for a year at least before giving up to despair, even if there be no apparent improvement in the muscles. The local temperature, usually very low, can always be raised several degrees by massage, and even if the muscular tone and voluntary movement are not restored, the increased activity of the circulation, which by persistent effort can be established, will make a great difference in the patient's comfort.

The direct influence of massage upon nutrition, the peripheral circulation, secretion, and excretion, the indirect effects upon the heart and upon respiration, combine to render it a most important aid in treating the protean aspects of *hysteria and neurasthenia*. Individual aspects of each case, in the way of sensory disturbances, disorders of digestion, and the like, may require special modifications in the application of massage; but for the most part what has already been described as "general massage" will be found the most useful. Combined with rest, full feeding, and isolation, it is an indispensable part of the "rest-treatment" of Weir Mitchell (13). For the details of the application of these means the original essay in which it was proposed may be consulted, or Dr. Playfair's book (14) by which it was introduced in England. Care must be taken at first not to overwork patients; but after a few days massage may be ordered for a full hour daily, or even, as Dr. Playfair has used it, twice a day. Especial attention should be given to the proper and thorough performance of abdominal massage, on which much of the patient's ability to take and digest food, as well as the regularity of the intestinal action, will be found to depend. A weekly weighing of the patient will tell whether massage is properly performed or not. If weight is not being gained some oversight will be found, either the diet is insufficient or imperfect, or the massage ill performed. Dr. Playfair is of opinion that the desire for food and the power to assimilate it is the best guide as to the efficiency of the rubbing. Another indication will be found in the urine, where the presence of deposits of urates or uric acid will quickly tell of mal-assimilation.

Patients with *melancholia* and various forms of *insanity* may advantageously be rubbed should the general indications call for it. Those often need it who refuse to take active exercise, or if forced out of doors drag listlessly about. Melancholia, occurring about the time of the menopause, has many of its most disagreeable symptoms greatly mitigated by massage; for instance, the flushing so often complained of in various forms is improved by the better balance of circulation which is brought about by manipulation.

Massage for gynæcological ends is a matter for a special treatise — at least so far as the direct manipulation of the uterus by Brandt's method is concerned. Its desirability is open to very grave doubts, although its utility seems to be established by the testimony of Profanter's reports of Schulze's cases (15), Bunge's (16) articles, and the studies of Reeves

Jackson (17) of Chicago. These authors have described successes in the treatment of the various forms of displacement of the uterus and its appendages, of hyperplasia, of chronic metritis, and most decidedly of pelvic exudates, para- and peri-metritis.

The technique consists in raising the uterus (and, so far as may be, its appendages) by a finger of the left hand in the vagina, by which it is held against the abdominal wall, where it is kneaded and pressed upon by the right hand. That such treatment may be of great usefulness in the removal of old inflammatory deposits, and restore tone to the uterine walls and to the ligaments, is evident from the effects of like manipulations elsewhere. Pregnancy, acute inflammation, and of course the presence of catamenia, are contra-indications. Further, it is obvious that such treatment can only be carried out by the hands of a physician, whether man or woman; and whatever the results may be, it is so tedious, fatiguing, and unpleasant to the performer, so annoying and painful to the patient, and open to so much abuse, that it is little likely to find favour.

Massage, in conjunction with other and more useful measures, may be applied to the reduction of obesity. Dr. Weir Mitchell, Dr. Goodell, and others have used it, together with a minimum quantity of food, to reduce the unwholesome adipose deposit of that very troublesome class of patients, the fat anæmics. By keeping them quiet in bed and giving nothing but skim milk in small amounts, weight may be rapidly and safely lost. [*Vide* art. on "Obesity."] Unusual or excessive local accumulations of fat may be removed by massage limited to the abnormal areas, and used with considerable vigour at short intervals.

There is a remarkable unanimity of opinion among those who have used it as to the value of massage in morphia habit, and the other forms of drug addiction. It should be used throughout the course of treatment whatever be the plan employed, and with special care during the collapse which almost inevitably follows the final withdrawal of the accustomed stimulus, be it opium, cocaine, chloral, or alcohol. The weak heart calls loudly for help in such patients, especially in the slaves of morphia; and as the stomach is apt to be very irritable, it is an advantage to have this means of strengthening the movement of the blood without risk of upsetting a feeble digestion. Moreover, it has a remarkable sedative effect, due in part, no doubt, to the resulting relaxation of the peripheral vessels and in part to its soothing influence upon the irritable nerves.

Though the conditions which render massage undesirable or impossible are implied in much that has already been said, a few words on the *contra-indications* may be added.

Acute skin inflammation, burns, unhealed wounds, in fact any break in the cutaneous surfaces, render the use of massage impossible, at any rate upon the affected locality; although, as has been stated, it may sometimes be employed in the neighbourhood for its derivative effects.

The presence of fever should act as an absolute prohibition on account of the rise of temperature induced by manipulation. Treatment may in

certain cases — in consumptive patients, for example — be used in the afebrile interval.

In all processes in which pus is formed, as well as in cases of malignant tumour, it is obviously undesirable to apply a means which may result in the dispersion of infective products into the tissues or throughout the system.

Weakened vessel walls from general causes, fragility of the arteries, or dilated veins, forbid deep kneading, though effleurage may be employed.

Pregnancy contra-indicates abdominal massage, though no hesitation need be felt in using muscle-kneading, and friction to the rest of the body up to a very late date in the period of gestation.

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J. K. M.

THE GENERAL PRINCIPLES OF DIETETICS IN DISEASE; OR, THE FEEDING OF THE SICK

THE best writers on medicine from the earliest times have been careful to include in their treatises some account of the conduct of diseases by means of diet; and, with the advancing changes and improvement in the art of medicine, the subject of dietetics has not failed to receive an increasing share of attention.

As in respect of treatment by means of drugs or other therapeutic measures, so here we find that many changes of opinion have occurred; methods at one time in vogue have been subsequently discountenanced, and at a later date again enjoined. It must be admitted that the whole subject of dietetics has rested on an empirical basis, and been destitute of any scientific principles till within the last half of this century.

With the progress of chemistry and physiology, and by more exact clinical researches, a truly scientific basis has been laid; we have now indeed attained a measure of certainty in respect of dietetics as an instrument of medicine which may fairly be counted amongst the triumphs of modern therapeutics. This work has been done by many labourers: it has required the combined efforts of the chemist, the physiologist, and the clinical physician; and in no other manner could such a task have been accomplished.

Dietetics have always formed part of any system of medicine, however peculiar or erroneous; and contributions to the subject have come from many, and sometimes strange sources, all tending to throw light on difficult and unillumined parts of it. Of this we may feel sure when we review the claims made for their several methods by those who have enjoyed high-living, low-living, "vegetarianism," hot-water drinking, total abstention from alcoholic liquids, and full stimulation with them; to say nothing of many varied and fantastic fashions in diet, all of which have been tried and fairly appraised. We have witnessed the results of so-called homœopathic treatment of patients, in which a large amount of attention is paid to diet, and feel that, in all fairness, it should be granted that at one time some accession to our knowledge of clinical dietetics came from this source.

In this article we are only concerned to set forth the **principles and practice of dietetics,** in so far as they relate to the needs of patients suffering from various diseases; and to illustrate their application in practice. This effort necessarily comprises a due consideration of the best methods of which we have now certain knowledge, and can only be grounded upon extended and carefully-weighed clinical experience.

In recent times less and less heed has been paid to drug-treatment, and more attention has been given to diet and general hygienic environment. This waning faith in drug-administration, which is unwarrantable and, to a large degree, unwise, has come of a fuller knowledge of the natural course of many morbid conditions. More reliance is placed on the *vis medicatrix naturæ;* and the art of the older drug-giving physicians has gradually fallen into desuetude, and ceased to engage the attention of many of the most capable minds in medicine. In the meantime, however, much certain knowledge has been secured, — knowledge which is absolutely necessary in order to guide our efforts successfully in relieving suffering and helping on recovery. It would plainly be beyond the limits of this article to attempt to discuss the dietetic treatment of each malady: it will suffice to lay down the principles, and to suggest the practical application of them in dealing with disease of the several systems of the body, referring more in detail to the more important general morbid states, and to the requirements of some special disorders.

I propose to discuss clinical dietetics in relation to the following: —

1. Specific Infectious Diseases; 2. Diseases of the Nervous System; 3. of the Respiratory Organs; 4. of the Circulatory Organs; 5. of the Digestive Organs; 6. of the Blood, Lymphatic System, and Ductless

Glands; 7. of the Urinary Organs; 8. Chronic Intoxications; 9. Diseases of the Locomotory System; 10. of the Skin; 11. Atrophy. Obesity I shall deal with in a later article.

I prefix a few remarks on **the Feeding of Helpless Patients.** Reference will frequently be made in the following pages to feeding of patients who cannot help themselves. This is conducted by means of a spoon, by the feeding-cup, or by the nasal tube. The best size of spoon, in the case of adults, is that known as the dessert-spoon, or small tablespoon, holding two or three fluid drachms; a teaspoon is the most convenient for

FIG. 32. — Feeding-cup with well-curved spout and india-rubber tube attached.

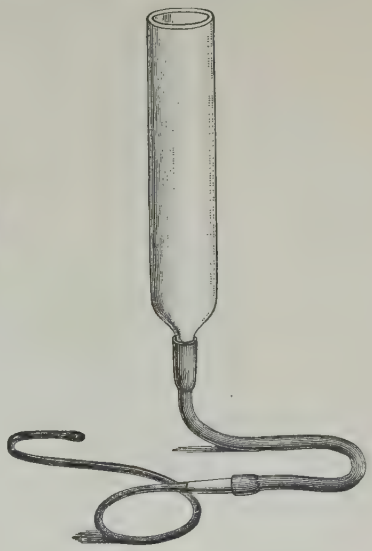

FIG. 33. — Apparatus for nasal feeding.

children. When the sensorium is dull, liquid nourishment is best introduced slowly at the side of the mouth. The best form of feeder is depicted in Fig. 32. The spout should be well curved, and it is often advisable to add a piece of soft rubber tubing to the end of it with a glass nozzle. Feeders with straight spouts are unsuitable; the contents of such feeders are apt to be shot out in spurts which may be spilt over the patient. Dr. F. M. Watt, of Edinburgh, has recently recommended a feeder with three handles as being easily seized by a recumbent patient—one right, one left, and one posterior, with a flattened tubular mouthpiece. The most useful form of apparatus for nasal feeding is that shown in Fig. 33. It is readily made by taking the barrel of an ordinary glass urethral syringe, and affixing to the nozzle a piece of soft red rubber tubing of a size suitable for passage along the floor of the nose, and about ten inches or a foot in length. This, after being well oiled, is passed along the nose in a line backwards towards the external auditory meatus, and slipped over the

posterior surface of the velum palati into the pharynx and gullet. This is a simple method, and even children soon become tolerant of it. The nutriment is to be poured from a small lipped jug into the glass barrel held up vertically over the patient's face. With this arrangement the progress of the fluid as it passes into the gullet can be accurately determined, and as much food as is necessary can thus be readily introduced at regular intervals. In cases of apoplexy, insensibility, melancholia, or other forms of insanity, and after tracheotomy, this method of feeding is of supreme value and importance. Half a pint to a pint of nutriment may be given at one time. A small piece of glass tubing may be introduced into the length of india-rubber tube to allow the transit of food to be observed.

Dietary in Specific Infectious Diseases. — A consideration of this subject naturally includes the dietetic management of the febrile state as such.

The condition common to all these temporary acute illnesses is that recognised as fever or pyrexia. *Pyrexia* is a symptom which is now acknowledged by many modern observers to be no longer an inimical, but rather a friendly process so long as it is restrained within certain limits.

In febrile conditions the alimentary system is more or less disturbed, almost without exception: the common indications of this are — first, the loss of natural appetite; secondly, the presence of thirst. Solid food is loathed, and if taken or pressed, commonly rejected by vomiting. The changes in the mucous surfaces tend to dryness and greatly reduced secretion from salivary and mucous glands, gastric tubular glands, duodenal (Brunner's) glands, Lieberkühnian follicles and the pancreas. The condition of the intestinal solitary and agminate glands when they are not specifically involved, is hardly known; nor that of the four million, more or less, villi of the intestine; but it may fairly be believed that these are in a more hyperæmic and sluggish condition, as regards normal absorptive function, than in health. Certainly, in most cases, we have clinically to note a greater or lesser degree of catarrh as pervading the entire course of the alimentary canal and of the ducts which lead into it; and we take heed to this condition in determining a diet for patients thus affected.

With respect to digestive capacity we particularly note the absence of sufficient saliva and pancreatic secretion on the one hand, and of gastric and intestinal juices on the other, and are thus in the presence of incapacity to deal effectually either with amylaceous food or with the several varieties of albumins. In the severer forms of prolonged fever, gastric digestion is commonly more in abeyance than that carried on in the intestines. Pyrexia thus reduces digestive capacity somewhat to that which is the normal state of the infant during the first six months of life, more particularly in respect of the inactivity of salivary and pancreatic functions.

In practice, however, it is possible to pay too much heed to these facts and, as in politics "the Queen's Government must be carried on,"

so here our patients must be fed and sustained through the exhausting conditions associated with and dependent on fever. Ample experience has proved the value of a diet consisting mainly of milk and meat juices. The points to attend to in such a dietary relate to the purity and dilution of the milk, and to the variety and quality of the meat juices. First, with respect to milk: it is of essential importance to employ fresh milk whenever procurable. Preserved milk, in all forms, is vastly inferior for nutritive purposes. As a rule, unless the source is beyond suspicion, fresh milk is best scalded, but not boiled. It is then to be diluted with barley water, or toast and water, to the extent of one-third or one-half. If diarrhœa be present lime water should be added, and half the amount of barley water may be thus replaced. If constipation prevail, the addition of sodium bicarbonate, instead of lime water, to the mixed fluids is advisable — one drachm (a teaspoonful) being stirred with each pint. These measures prevent the formation of curd in any but a finely-granular condition, and so prevent pain, flatulency and intestinal disturbances. When milk is badly borne whey is often available, and to it cream may be added if desirable.

Beef juices may be given at intervals in the form of well-made beef tea, mutton tea, chicken or veal tea; or, occasionally, if the stomach be queasy, in the form of essences, of which there are now several trustworthy preparations. Fresh beef essences, if they can be procured, are probably better than any of the latter; and vegetable juices may be incorporated with all forms of these by immersing in the cooking-vessel a muslin bag containing finely-divided vegetables such as cabbage, carrot, etc., and so securing variety both of flavour and nutrient elements. A good rule is to change the meat juice from day to day, so as to prevent the monotony of the spoon-food. Nothing better relieves such monotony than the regular administration of draughts of iced water which are always grateful to fever patients and are too often omitted. In many cases both tea and coffee may be given with advantage. Refreshing drink is available in most febrile states — enteric fever and rheumatic fever excepted — in the form of freshly-made lemonade containing a drachm of acid tartrate of potash in each pint, and a very little sugar. Regard is to be paid to the amount actually consumed, and care taken that enough is presented in each twenty-four hours. Modern skilled nursing commonly secures this, and a register is to be kept from hour to hour. Fruit is sometimes of use, and cooked apples may be given, carefully prepared, also grapes and oranges. In small-pox the latter are especially grateful. Whenever it is advisable to add to the nourishment, yolks of eggs may be added to milk or beef juice, or given with brandy as egg-flip.

We have thus considered the essentials of a so-called fever diet. The question of alcoholic fluids now presents itself. These form no routine part of dietetic treatment either in febrile or in any other morbid condition. They may, however, be necessary, and are often indispensable, in the conduct of particular cases. The skill demanded in the prescription of alcohol (that is, of alcoholised fluid of whatever kind) is of the same

order as that which is required in determining the use of any other article of food or medicine for the sick. We do not affirm that because the patient has fever, or has pneumonia, he therefore requires wine or spirit. He may or he may not. We are guided by various considerations as to the specific requirements of each patient, and we give or we withhold as the case may be. We lend ourselves to no fashion or wave of opinion in respect of food or drugs, and study the precise indications of the case for the time being. The opinions to be here stated are the result of no small experience, and have been gathered only at the bedside.

We are met at the outset by those who contend that alcohol is not a food, and has therefore no place in any dietary. We might put this opinion aside, and still contend that it has a high place in the treatment of disease. As clinicians we maintain, however, that alcohol is practically available as a food, even in the form of a pure spirit; and if the several constituents of wine be taken into consideration we have to deal with a variety of nutrient materials in subtle combination, with which alcohol, in moderate percentage, is bound up. We recognise that alcohol holds an intermediate place between carbo-hydrates and the fats, being less oxygenised than the former and more so than the latter. In its circulation through the system, within certain well-understood limits, it becomes destroyed and indetectible; we must therefore believe, as physiologists, that this process of destruction and transformation is attended by oxygenation and a correlative liberation of energy. We may thus explain some of the benefits derivable from the use of alcoholised fluids in various morbid states.

The *clinical indications for alcohol in febrile states* are now fairly well understood and reduced to principles. It is recognised that if no extreme pyrexia be present, if the action of the heart continue sufficiently vigorous, and food be well taken, alcohol is unnecessary. But if high fever prevails, the heart's action falters, and ordinary nutriment is taken with difficulty, at any age, and in any such case, alcohol is indicated, and its effects are under such conditions uniformly satisfactory. Thus by its use we control pyrexia, we sustain the action of the heart and the vigour of the circulation, and we secure a substitute for other nutriment till such time as a better appetite returns. We gather all these indications from the thermometer, the stethoscope, the character of the pulse, and the capacity for taking nourishment. The best form for alcoholic administration is either that of brandy or whisky well diluted with milk. Neither should be given with beef tea or any meat juices, and the quantity is best administered at regular intervals of two or four hours, according to the particular indications, both by day and by night. The amount required is to be determined by the age and previous habits of the patient, and no less by the conditions requiring to be met. Young children bear alcohol well when it is indicated; and the amount sometimes called for may be very large. In practice it is seldom found necessary to exceed for an adult of average condition in any febrile state six ounces of brandy or whisky per diem, and two or three will often secure all that

is needed. Over-stimulation is harmful, and is recognised by flushing, foul breath and discomfort. Hyperpyrexia demands the use of alcohol, and the patient is benefited by it. The cardiac indications for the use of alcohol in fever are a notable loss of tone in the first sound, especially if this be inappreciable at the base (Stokes' sign), and the associated condition of pulse that of low arterial pressure, and the phase of it known as dicrotism. The tendency to formation of sordes on the tongue or gums in grave febrile states also indicates the employment of alcohol.

Preparations of malt are certainly available in febrile conditions, and are agreeable to patients. Granulated malt extract dissolved in warm water or milk constitutes a grateful variety of readily digestible nutriment when the constant use of milky food palls on the appetite.

When the stomach is irritable, and most of the food already indicated disagrees, recourse may be had to koumiss in small quantities (Koumiss, No. 2). Milky food may sometimes be better borne if given in doses of half an ounce to an ounce every quarter of an hour by the clock. After a few hours larger quantities may be tolerated.

The dietary thus enjoined is available for most febrile conditions, however induced, including pneumonia, all the exanthemata, and the continued fevers, with the exception of enteric fever, to which reference will presently be made. The same holds good for paroxysmal stages of remittent and intermittent fevers, allowance being always made for the degree of pyrexia, the age, and bodily state of each patient.

Certain precautions are of extreme importance in the case of *enteric fever*, the specific conditions of the intestinal tract from day to day being always borne in mind. The necessity for introducing only bland and unirritating nutriment is paramount. Hence the importance of preventing any masses of milk-curd from passing through the pylorus which may chafe or lodge upon ulcerated patches in the ileum and colon, and induce diarrhœa or constipation. Attention is further necessary to prevent fruit in any form being administered by injudicious attendants or friends. Lemonade is to be forbidden, and all wines, for these are distinctly apt to promote action of the bowels. Vegetable juices may be introduced, as already indicated, with meat juice. Alcohol is only permissible in the form of brandy, whisky, or gin. These matters appear to smack of pedantry, but the rule enjoined has been dictated by the amplest experience, and no point, however small, is unimportant which may turn the scale in favour of life or death in these terrible cases. Lives have been needlessly sacrificed by inattention to or inappreciation of matters seemingly trifling such as these.

It has been freely asserted of late that milk is an inappropriate food in enteric fever, inasmuch as it is a pabulum highly favourable to the growth of the specific bacilli of the disease, and it has been urged that preparations of malt are much safer. Indeed, Dr. Springthorpe, of Melbourne, has strongly urged the use of a sterilised hopped malt

extract, which resists the growth of Eberth's bacillus in cases of enteric fever.[1] The value of malt has been already noted. The disadvantages of milk, properly diluted and alkalised, are, however, by no means proved, and it would require very strong evidence to convince careful physicians that it is not a satisfactory basis of diet in these cases. Voit asserts that three and a half pints of milk *per diem* are insufficient for nourishment in a case of fever, there being a lack of albumin, twice too much fat, and deficiency of carbo-hydrates by two-thirds. Further, that even with the addition of animal broth such a dietary is inadequate. Clinical experience does not justify the acceptance of these statements. The average patient, as a matter of fact, does very well on such a diet; and beef tea or mutton tea may be fortified with essences of one or other as required.

It is found that where diarrhœa is a prominent feature of the illness, beef tea or beef essence may act as a peristaltic stimulant, or otherwise as a purgative; whereas mutton tea and essence, veal broth and chicken broth have no such effect, and it is a good rule of practice to attend to this point. In cases, not uncommon, where constipation prevails beef juices may be used, and sodium bicarbonate, rather than lime water, should be added to the milk. In rebellious diarrhœa, or where hæmorrhage occurs, milk is better avoided and whey employed, the latter in the form of alum whey, made by adding one drachm of powdered sulphate of alumina to each pint of scalded milk and straining through muslin. Mutton essence is best in such cases.

The greatest care is called for in the dietary during convalescence from this disease, no solid food, or nutriment entailing débris, being permissible for many days after all fever has passed away. Ordinary diet may be resumed at once in cases of typhus fever or in pneumonia, but not in enteric fever. We do well to begin with milky arrowroot, with yolk of eggs in milk or brandy and water, then to pass on to boiled pap of bread-crumb and milk, custard pudding, and lightly-boiled fresh egg. Next, pounded fish may be cautiously given, pounded mutton or beef in *purée*, rusks soaked in tea or milk, and so on to fish of delicate fibre, mashed potatoes, etc. In all cases it is better to be too late rather than too early in reinforcing the dietary.

Typhus, Relapsing, and other Fevers. — In arranging the dietary for patients suffering from typhus and other continued fevers, no special precautions, such as are of imperative necessity in enteric fever, have to be taken. The indication is to meet the exhausting character of the febrile processes by the introduction of such food in liquid forms as the patient can take, and with the abatement of symptoms following on the crisis solid food may be safely given, care being taken not to overload the stomach by excessive amounts, the appetite being large. The indications for alcohol are the same as in enteric fever, but wine may be safely given, or malt liquors if preferred. Good wine, of which mature port, Burgundy, or Bordeaux are the most desirable, is as a rule preferable

[1] *Australian Medical Journal*, 22nd July 1894.

in febrile exhausting conditions to pure spirit. The æthers of old wine are especially sustaining to flagging cardiac action, and the associated salts in wine are further beneficial. Champagne of good quality is useful in many cases when other wines are distasteful, but it can seldom be safely employed in enteric fever. There is no routine treatment in any case, and in early life, and in constitutions otherwise sound, it is sometimes unnecessary to resort to any alcoholic support, either during the fever or the convalescence from it. Each case must be judged by itself, and a well-trained clinical observer gives or withholds stimulants as circumstances indicate. Elderly patients, as a rule, need stimulants earlier and in larger amounts than younger ones. Typhus fever is almost certainly fatal after the seventh climacteric, whatever the treatment. Habitual drunkards, under the stress of continued fever, require sometimes very large amounts of stimulants. The tendency to collapse after the crisis in relapsing fever demands free stimulation, especially in elderly patients.

Exanthemata. — In the exanthemata the dietary is that for the pyrexial state generally. Later complications may occasionally demand moderate stimulation and a generally supporting diet, the condition of the kidneys in scarlet fever demanding especial attention.

Sterilised Milk; Boiled Milk and Water. — No reference has, so far, been made to the employment of sterilised milk, or of peptonised milk and animal broths. As to the first, it is a good rule to scald all milk, unless the source and treatment of it be certainly beyond suspicion: this holds good not only in India, but all over the world. The same may be affirmed for water under all conditions, and in India and in most parts of the world the rule holds good, especially in the case of children and young adults.

Peptonised Foods. — With respect to peptonised food I think there is now too great a tendency to employ it. All articles of diet come best *direct from nature*, as far as possible; and without more chemical or culinary meddling than is absolutely necessary. Food is one thing, physic is another. I feel sure that peptonised foods are now too frequently administered, and are often unnecessary. They have their place, without doubt, for gastric and for rectal alimentation as a temporary measure, the object being to present predigested albumin for rapid assimilation when digestive power is at a minimum, as malted foods present predigested starches in cases where salivary and pancreatic secretions are inadequate; but it has become a fashion to resort to the use of predigested food in many cases which do not require it. Most cases of pyrexia can be treated successfully without peptonised food, but if the digestive powers be enfeebled, it may certainly be used. The liquor pancreaticus is probably one of the best agents to employ in peptonising milk, animal broth or gruel.

Parotitis. — In cases of mumps spoon-food only is to be given, and generally in a concentrated form, the act of deglutition being painful.

Pertussis. — In whooping-cough nourishing diet is necessary. Vomit-

ing is frequent after paroxysms, but the patient is commonly ready to replace what is lost.

Influenza. — There is loss of appetite in the primary stage. But soon the specific depression of this malady necessitates the use of a supporting dietary in any desirable form, and alcohol is required, sometimes in large amount, to counteract the tendency to asthenia and cardiac failure; especially in elderly persons with pulmonary complications, and during convalescence which may be very prolonged. Yolks of eggs with brandy, strong soups, oysters, and pounded meat are suitable forms of nourishment, also strong coffee with plenty of milk.

Malarial Fevers and Yellow Fever. — In the intervals between the paroxysms it is desirable to employ a supporting diet. Alcohol is best given well diluted, and diluted champagne is valuable.

Dysentery. — Few diseases call for more skill and discretion in feeding than dysentery. In simple and acute forms the diet must be fluid, and the same holds good for many cases of the chronic form. It is common to find milky and farinaceous food recommended and weak animal broths. Without doubt milk should be the staple aliment, and it may be given alone for weeks together, diluted with warm toast and water and lime water. My reading and experience lead me to recommend nothing else. Beef tea is distinctly to be avoided. Veal or chicken broth are the least harmful of animal broths, and the yolk of eggs may be added. An adult will need four or five pints of milk diluted, as advised (three parts of milk, one each of barley water or toast and water and lime water), in the course of twenty-four hours. And it is to be borne in mind that neither diet nor drugs will be of any avail without strict confinement to bed and the use of draw-sheets for defæcation. No vegetable food or fruits are admissible, and starchy food is undesirable; in chronic cases freshly-made bael jelly or extract in drachm doses twice a day is allowable. Food should be administered warm, to prevent too active peristalsis. Alum whey is useful as an alternative when milk diet has to be long submitted to, and the mouth should be washed out occasionally with warm boracic lotion.

Erysipelas. — Supporting and stimulating diet is necessary. Milk and animal broths, containing plenty of salt, with brandy or port wine are to be given.

Diphtheria. — The main indications here are for a supporting diet. The chief difficulty arises in the cases of infants or young patients. The tendency is to collapse and cardiac failure all through the illness and early convalescence. After tracheotomy, which is necessary in the majority of cases of the laryngeal form, feeding can often be carried on only by means of the soft rubber nasal tube, and by this means many lives have undoubtedly been saved which would otherwise have perished from inanition. Milk, yolks of eggs, chicken essence and brandy, are almost always required. Young children bear brandy well given in milk, and it may be needed in divided doses in quantities varying from one-half to two ounces in the twenty-four hours. The presence of albu-

minuria is no contra-indication to its employment. From two to four ounces of milk, etc., may be given by the nasal tube at intervals of three or four hours by day and night; medicines also have to be given with the food in this manner. Sometimes the nasal tube may be dispensed with, or it may be advantageously used for a few days after tracheotomy.

Asiatic Cholera. — In the algide stage it is of no avail to press nourishment, everything taken is rapidly ejected. Sips of iced water or pieces of ice may be given to suck. In the stage of reaction small quantities of milk and soda-water, with bicarbonate of sodium, may be given in small amounts at stated intervals, and water arrowroot is admissible, a gradual return to very light food being cautiously carried out.

Syphilis. — The indications in all stages of syphilis being to secure the highest attainable level of the general health, good diet is necessary. The continued use of mercury or iodide salts still further necessitates this course. So-called diet drinks are of extreme value. None is superior to a pint or more of a good compound decoction of sarsaparilla taken in the course of each day.

Hydrophobia. — In this disease feeding must be carried out by nutrient enemata, and remedial agents are conveyed by the same means, or hypodermically. Swallowing may be possible towards the end of the case, and food be thus freely taken, too late, however, to save life.

Tetanus. — Feeding presents great difficulties here. It is best conducted by the use of the nasal tube, or advantage may be taken of a gap in the teeth to insert liquid nourishment. Rectal feeding is apt to induce spastic paroxysms. Alcohol is necessary, sometimes in large quantities. [*Vide* art. on "Tetanus."]

Dietary in Nervous Diseases. — *Neuritis: (a) Gouty, (b) Alcoholic; Sciatica.* — In cases due to gouty influence the diet is that proper for the gouty state present at the time. This will vary according to age, previous habits, and the vigour of the constitution. In alcoholic neuritis a plain nourishing diet is necessary, and complete abstention from all alcoholic fluids.

Diseases of the Spinal Cord; Bulbar Paralysis. — A generous, readily digestible diet, containing an abundance of milk and fatty elements, is required in these cases. In bulbar paralysis constant supervision is necessary to prevent choking. A soft tube should be passed into the stomach and liquid food injected as often as it can be tolerated. Failing this, nutrient enemata must be employed.

Cerebral Hæmorrhage. — Liquid food is to be given by the mouth if there is power to swallow; otherwise nutrient enemata must be used. No stimulants are to be given. On recovery the diet must be light, consisting of fish, milk, vegetable and farinaceous foods. In many cases the renal condition demands careful study in respect of diet.

Embolism and Thrombosis of Cerebral Arteries; Endarteritis; Atheroma. — In most convalescent cases it may be necessary to administer more nourishing food and stimulants in small quantities: the conditions

of the heart and circulation are the guides in this respect. The age and general state of nutrition must also be considered.

Epilepsy. — In patients subject to epileptic paroxysms much benefit is derivable from carefully-prescribed diet. This should be so arranged as to prevent any overloading of the stomach, and all food difficult of digestion is to be withheld. The principal meals are best taken in the earlier part of the day, and only a light meal consumed in the evening. Experience clearly indicates that a diet not too rich in albuminoids is advisable. Animal food should be sparingly taken, but fish may be used freely. Butchers' meat is better given on alternate days, if at all, and never in large amount. Farinaceous foods and fat are desirable. Milk in large quantities is harmful. Alcohol is better dispensed with, or very sparingly taken in the form of diluted light wines. Butter, cream, and fat bacon may be taken freely, and butter-milk in moderation has been found useful. Coffee and cocoa are commonly preferable to tea. There can be no doubt that recurrence of paroxysms may be materially checked by strict attention to the points just noted.

Migraine. — Few disorders are better controlled by careful dieting than this. There is distaste for food during the paroxysms. Iced aërated water is sometimes helpful in the attack. Tea and coffee are also sometimes of avail. There is a gouty element in many cases, especially in females, and errors of diet leading to goutiness may induce migraine in such persons. In the intervals between attacks regard must be had to this fact, and to the "growing-up" tendency to outbursts of varieties of paroxysms. More water drinking is desirable, and a strict limitation of animal and rich foods. Abundance of well-cooked green vegetables, such as spinach, is important. Malt liquors and strong wines are not to be taken.

Chorea. — In acute cases only "spoon-food" is to be given. At the height of the disorder nasal feeding may be necessary. Abundance of nourishment is necessary, and wine is usually beneficial. The rheumatic nature of the disorder (as held by the writer) does not in this case forbid the use of animal broth, but milk appears to be the most suitable form of nourishment. Assiduous attention on the part of the nurse is needed to secure a sufficiency of liquid food in grave cases. In milder cases care must be taken to prevent the patient suddenly bolting any masses of unmasticated food.

Hysteria; Anorexia nervosa; Vomiting; Refusal of Food. — The different and multiform phases of hysteria demand special attention in each case. The main principles relate to the use of a sufficiently nourishing diet, care being taken to avoid incautious resort to stimulants. Loathing of certain foods and many idiosyncratic vagaries may be encountered. These must be overcome as far as possible, or substitutes for any one of them provided. Aversion from red meat and from fat is not uncommon. Firm but gentle discipline is often needed to secure due nutrition. Morbid cravings demand special study, and the practitioner must beware of becoming an inflexible *doctrinaire*. There may be digestive capacity

for articles of food theoretically reckoned as unfit. Thus, lobster and pork may be desired, and beef, mutton and fish found repulsive. Complete anorexia is occasionally met with, and "fasting girls" may come under notice. These "phenomena" are not to be watched with vulgar curiosity, but the miserable subjects of them are to be forcibly fed, if necessary by the tube, and medically treated. Remarkably good results have accrued from such treatment in the hands of Weir Mitchell and others who have followed this method. Seclusion from friends and ordinary environments, with rest, massage, and enforced meals of strong soup, milk, cream, eggs and pounded meats constitute this method. Its great demerit is its costliness, which render it unavailable for any but wealthy patients, and, unfortunately, the good results are not always permanent. The infirmity of will, and the general instability of the nervous centres, have to be dealt with, and such patients, though much has been secured for them of late years, — and they tend to grow more numerous with what we are pleased to call "civilisation," — mostly remain objects of pity, and a sore tax both upon their friends and their medical attendants.

Hysterical vomiting and dysphagia demand the disciplinary use of an œsophageal bougie, rectal alimentation being carried on, or nasal feeding, the bougie and nasal tube being subsequently threatened *in terrorem*.

Neuralgia. — Generally speaking, supporting diet is called for. If neuralgia be "the prayer of the nerve for healthy blood," that prayer must be answered. We distinguish between nerve pain due to specific morbid condition, capable of removal, and that due to lowered vitality and exhaustion with poverty of blood. Thus gouty, syphilitic and diabetic neuralgias have to be considered, and appropriate dietetic measures adopted for each. In the neuralgias due to exhaustion we have to insist on a full supply of digestible food with plenty of fatty elements. Butter, cream, Devonshire cream, and fresh unburnt fats are thus of value. Post-catarrhal and influenzal neuralgia, the miserable paroxysms of pain in affections of the fifth and occipital nerves, and post herpetic (zonal) neuralgia are often benefited by the temporary free use of mature port wine, best taken with meals.

Disease of the Respiratory Organs. — *Tubercular, Syphilitic and Cancerous Laryngitis.* — In advanced cases of any of these diseases feeding becomes difficult and painful. Spoon-food is necessary, and the most nourishing fluids must be given. Yolks of eggs, milk thickened with arrowroot, and thin jellies are suitable. Care has to be taken that no food enters the larynx. It is sometimes advisable in painful cases to paint or spray the pharynx and glottis with a solution of cocaine (to be freshly made every week, 5 per cent strength) five minutes before attempts are made to swallow. A soft tube may have to be passed into the œsophagus to conduct liquid food in these cases and in the sensory paralysis dependent on diphtheria and bulbar disease.

Bronchitis: (*a*) *acute*, (*b*) *chronic.* — The diet should be light and

nourishing in acute bronchitis. In chronic bronchitis the patient commonly requires strong nourishment and abundance of fatty food. Alcohol in some form is generally useful.

Asthma. — The diet is often an important element in successful treatment of these cases. Indiscretion and inappropriate diet often induce paroxysms. Small meals of readily digestible food are best. Many idiosyncrasies are met with respecting tolerance or intolerance of articles of diet. I have known fresh butter to be constantly and immediately provocative of an attack. Hard meats, cheese, pastry, beer and ill-cooked food are generally inadmissible. Full evening meals are to be avoided, and the chief meal is best taken early in the afternoon.

Emphysema. — The chief point to guard against is the use of any food that may create flatulent distension of the stomach and bowels.

Pneumonia. — The diet here is as for fever till the crisis occurs. After this the patient may have solid food if desired, and the amount of liquids be somewhat restricted. Alcohol may be required, as in fever, and is often beneficial. It may have to be freely given in elderly persons and confirmed hard drinkers. The onset of *gangrene* is the signal for free stimulation, strong meat essences and milk.

Phthisis Pulmonalis. — The indications in all forms and stages of pulmonary phthisis in respect of diet are to supply as much digestible nutriment as can be disposed of. The condition of dyspepsia which is often concurrent needs appropriate dietetic treatment. The meals should be smaller and more frequent than in health. All varieties of flesh, fowl and fish, with abundance of fatty food, are proper. Milk is of great value. An early breakfast in bed is often advisable, consisting of tea made with cream, or instead, half a pint of warm milk with the yolk of a raw egg stirred into it. Where night-sweats are present, a cup of cold tea made with cream, or two ounces of claret and water, may be taken on awaking at four or five o'clock in the morning. Malt extracts are certainly of use, and may be given in warm milk. Diluted warm drinks of nourishing quality aid in promoting free expectoration and lessen harassing cough. Malt liquors are excellent if they can be digested. Failing these, any form of alcoholic liquid taken with meals is advisable. Half an ounce of rum taken in half a pint of milk is a well-approved combination taken early in the morning, and again in the forenoon. Eggs, oysters, sweet-bread, fat bacon and tender ham, roe of fish, caviare and brains, are all useful in varying the diet and encouraging languid appetite. In early cases of phthisis there is no better midday meal than a large fat mutton chop, grilled, and half a pint of good draught porter. Junket and Devonshire cream with custard pudding or stewed fruit may be taken. The presence of tubercular enteritis demands the diet found useful in diarrhœa or dysentery, the curds of milk being harmful and solid food unsuitable. Alum whey and koumiss may be of service in such cases, and mutton or chicken essence preferable to beef essence. To promote good digestion of suitable nourishment is to secure the first line of defence in resisting the progress

of tuberculosis in any part of the body, and no therapeutic measures are of any avail in default of this. A great modern error is to be guarded against. It is now sought to combine food and physic in numberless preparations foisted on the practitioner by manufacturing chemists. These are mostly nauseous and harmful. It needs good judgment to keep well apart food, which is to be enjoyed if possible, and physic, which is to be tolerated only so far as is necessary. Too often one finds the stomach oppressed by continual alternations of food and physic, and the end sought is not attained. Simplicity and orderly method will accomplish much more than an elaborate and fanciful scheme of diet; and, certainly, in the earlier stage of phthisis the patient must not be too much regarded as an invalid to be coddled and stuffed. We have to seek robustness, and to cultivate all the bodily powers of resistance.

Coryza; Common Colds; Febrile Catarrh. — In ordinary catarrhal states of the nasal, faucial and bronchial mucous surfaces, there is hardly any justifiable interference with the usual diet. In severer febrile attacks a slop diet is advisable, and alcohol should be withheld. It is a common error to over-feed and over-stimulate in this condition. Animal broths, well salted, milky and farinaceous food, with plainly-cooked vegetables, are best. Lemonade, freshly made, and taken hot at bedtime is an approved remedy, and tamarind tea, barley water sweetened with liquorice, and linseed tea, are all useful varieties of diluents. A diet restricted in liquids has been recommended, but has found little favour. During the course of a progressive febrile process diluents are in many ways advisable.

Diseases of the Organs of Circulation. — *Inflammatory Conditions of the Heart and Pericardium.* — In these cases we have practically to do with the conditions which underlie and induce the several disorders in question. These relate to the peccant matter of rheumatism, to morbid blood-states in renal diseases, and to specific toxæmia due to bacillary invasion.

The diet proper for patients with cardiac complications of rheumatism is mainly that for febrile states, except that animal broth is harmful. Milk properly diluted and farinaceous food only are allowable. Rusks and biscuits soaked in milk, bread-pap, arrowroot, simple nursery puddings (without eggs), and mashed potato may be given. In pericarditis with effusion the diet should be restricted somewhat in respect of fluids, and all sources of flatulence be avoided. The pulse condition will determine the employment of alcohol.

Malignant (Ulcerative) Endocarditis. — In malignant endocarditis stronger nutriment is necessary, and animal broths, eggs and pounded meat may be given, and spirit or wine will commonly be needed.

Myocarditis. — Myocarditis calls for the use of alcohol whenever recognised. In simple rheumatic pericarditis stimulants are best avoided as far as possible.

Pericarditis in Bright's Disease. — In these cases the condition of the kidneys determines the diet. These organs are inadequate to the performance of their functions, and can ill bear any undue work thrown upon them. A milky and farinaceous diet is suitable; lemonade or imperial drink are useful; so likewise are whey and koumiss. Vomiting may be a serious complication, and, in any case, the prognosis is as grave as can be.

Valvular Diseases of the Heart and Complications; Hypertrophy; Dilatation. — The main objects are to give sufficient supporting food, but to ensure its digestion with comfort, and never to overload the stomach. Gastric and intestinal catarrh are often present, and a light diet is then imperative. The condition of the kidneys must always be considered together with that of the circulation, and no less the state of the pulse in respect of arterial tension. Alcohol is commonly useful and necessary, and no form of cardiac valvular disease *per se* contraindicates it; in aortic reflux it is generally advisable, especially in advanced stages, and some should be given at bedtime in addition to that taken with meals. When hypertrophy of any cavity is sufficient, especially in young persons, there may be no need for alcohol. When dilatation sets in alcohol is valuable. In the latter condition it is well to restrict the amount of fluid taken, a "dry diet" being advisable and productive of much benefit. Four or five small meals may be taken in the course of the day, and liquids taken after them. Whey, milk and lime water, or milk and bicarbonate of sodium, are useful when nausea and anorexia are present, with engorged liver and acute gastro-enteric catarrh. Prudent medication in these conditions much aids the appetite. Imperial drink is of service, and fresh or well-cooked fruits are admissible. Coffee and cocoa are generally better than tea, though the latter is well borne by many people if not too strong.

Congenital Malformations. — In these cases gastric catarrh is apt to recur, and the diet must be adapted to this condition. The digestion is feeble, and very plain food suits best. Alcohol is only needed for cardiac failure in the later stages.

Functional Heart Disorders. — Overloading of the stomach and even a discreet use of tea and coffee may cause or aggravate some of these. Alcohol is not advisable in tachycardia, and in many cases of infrequent and intermittent cardiac action it is unnecessary. Each case requires special study.

Angina Pectoris. — In this disorder care must be taken to provide small and digestible meals, especially towards evening. The specific character of each case must determine the employment of alcoholic drinks.

Exophthalmic Goitre. — The same rules apply here as in the two foregoing conditions. Vomiting and diarrhœa often need special care.

Aneurysms; Arterial Degeneration. — Much benefit is to be derived from a more or less close practice of Tufnell's dietetic treatment. This is not available for elderly patients, or for persons with aneurysm and

aortic reflux, and in very few cases is it a successful remedy. One main principle of the plan consists in a small intake both of fluids and solids, the chief benefit being probably derived from the reduced amount of fluid. Eight ounces of fluids and ten of solids may be enjoined for several weeks on a bedridden patient; a water-bed and a bed-pan are imperative. In summer this restriction is often found intolerable, thirst is common, and constipation the rule. Two or three ounces of port wine form part of the fluids. The latter have often to be increased, and towards the end of six or eight weeks the whole diet is gradually increased. A modification of this system is found to answer well in most suitable cases. Some lemon juice is necessary in addition to this dietary.

The subjects of arterial decay are to be sparingly fed, but some wine is commonly advisable, especially in elderly persons. The condition of the kidneys must be carefully ascertained before enjoining a diet.

Thrombosis ; Embolism. — The particular feeding of patients with thrombosis of veins will depend on the conditions which caused it. In anæmic persons good diet is necessary, with alcohol. In gouty persons a very plain diet is imperative, and alcohol, if required, is best given in the form of diluted spirit. Abundance of green vegetable, such as spinach, is useful, and any cruciferous vegetable. Water drinking and diluents are important.

The presence of arterial embolism commonly demands a good diet, with some alcohol, especially in elderly patients.

Diseases of the Digestive Organs. — *Stomatitis.* — Fluid nourishment is alone to be employed in all forms of stomatitis. Milk and sodium bicarbonate is best, and should be given tepid or warm. Milk arrow-root, and a little brandy with it, is useful. Yolk of egg with milk is admissible. After feeding, the mouth should be washed out with warm boracic lotion.

Tonsillitis. — Supporting liquid nourishment is to be given. Milk, beef essence, yolk of eggs, and port wine are best; and in severe cases these must be firmly pressed in spite of painful deglutition. Nutrient enemata may be required for a time.

Œsophageal Obstruction. — Concentrated liquid food is best, and when this no longer passes, nourishment must be given by a small tube, with a funnel-shaped end, worn in the gullet, its lumen being kept patent by a cat-gut bougie, both being affixed to the side of the mouth by diachylon plaster (Symonds' and Berry's method). Rectal feeding is usually necessary in addition, or by the stomach directly, if gastrostomy has been performed.

Gastritis (acute). — Nutrient enemata are best, perfect rest being given to the stomach. Milk and soda water and small pieces of ice may be given by the mouth after twenty-four hours. Subsequently, milk and sodium bicarbonate, with barley water, custard puddings, and yolks of eggs.

Gastritis (chronic). — Only the most digestible and bland nourish-

ment is advisable. Tea, coffee, and alcohol are inadmissible. Milk and farinaceous food, soft fresh fish, pounded meat, mutton, chicken, mashed potato, and lightly-boiled fresh eggs may be given in small quantities. Sugar is inadvisable. Nourishment is to be given at regular and not too long intervals — every three or four hours.

Dyspepsia, Varieties of. — Each case must be specially studied. Generally the diet is as for chronic gastritis. Many idiosyncrasies may be noted in respect of tolerance and digestive capacity. Alcohol will aid in some forms, given with or just after a meal, and painful dyspepsia will sometimes yield to a few spoonfuls of hot brandy or whisky toddy at the end of a meal. Many cases do best without alcohol in any form. Malt liquors are generally inadvisable. Excess of bread-eating is sometimes harmful. Toast or "pulled" bread or biscuits often well replace bread. Browned and over-cooked fats generally provoke acid dyspepsia, and all rich, twice-cooked, or highly-seasoned dishes are inadmissible. Small meals, no second helpings, avoidance of soups and of much liquid with meals, are points to be attended to. All vegetables should be sparingly used, and cooked as a French cook always — and an English cook never — cooks them. Indulgence in the sweet courses is a fertile source of acid dyspepsia, and indigestion of amylaceous food leads to the same in more cases than is generally supposed. Boiled fish and plain roasted and grilled meats are generally well digested, also custard pudding and light omelettes.

Recumbency is to be avoided after meals, and no brain-work undertaken during or soon after them. Solitary meals are disastrous, and that customary, but very unwholesome, combination, the tea-dinner, is to be avoided. No meals should be taken after eight o'clock in the evening. Very weak tea or some hot water may be taken an hour after the evening meal. A glass of water may be slowly sipped at bedtime, but no alcohol is permissible with it. Further details cannot be set forth here. No food is advisable between meals, and full intervals of rest must be secured for the digestive organs. Many strange dietetic methods for treating the varieties of dyspepsia are in vogue. Of all of them I will only affirm that they are unwarrantable, and that common sense and experienced clinical skill will effectually secure all that is attainable for the permanent welfare of the patient.

Gastric Ulcer. — Rest to the stomach is the key-note of treatment — nutrient enemata alone being employed for some days. A little water by the mouth or pieces of ice may be taken, but even this may be inadvisable if vomiting be urgent, or hæmatemesis have lately occurred. Afterwards, whey, or milk with lime water and barley water, may be given, in tablespoonful doses, each quarter of an hour by the clock. I object to peptonised food in these cases, as the ulcer may be injured and checked in healing thereby. Subsequently, milk arrowroot, yolk of egg, biscuit powder and milk in thin pap, bread crumbs and milk in fine pappy condition, and milky cocoa (without sugar) may be given. Beef essence, liquid jelly, pounded fish, pounded chicken or mutton may next be tried,

once in each day, and the effects carefully noted. Vegetables, fruits and alcohol are to be avoided. Strict confinement to bed is absolutely essential.

Cancer of the Stomach. — The diet is as for ulcer of the stomach. Peptonised foods, however, are admissible when there is no vomiting, pain or hæmorrhage, and pultaceous or even solid food may be remarkably well borne. Light wine, champagne, dry Moselle wine, or port wine may be employed. A teaspoonful of neat brandy sometimes much relieves pain in these cases. When vomiting is rebellious, iced foods and well-aërated waters may do good. Some patients tolerate an ordinary mixed diet very well if the pylorice orifice is free.

Pyloric Stenosis from cancerous or simple over-growths ; Gastric Dilatation. — The diet here is as for chronic gastric catarrh. Dilatation from pyloric stenosis leads to retention of contents, and to fermentative decompositions, growth of sarcinæ ventriculi, etc. Washing out of the stomach daily or every second day, before the principal meal, is of great value, and amylaceous food is to be much restricted. Beef essence, yolk of egg, custard, pounded meat, jellies and milk, with some diluted alcohol, are admissible. Much fluid is undesirable, and a somewhat dry diet is to be enjoined.

Intestinal Diseases; Enteritis. — The food should be the same as for gastric ulcer, and not taken too hot.

English Cholera ; Cholera nostras. — Milk and barley water with a little brandy are best when the vomiting subsides. Chicken and mutton broth are preferable to beef tea.

Infantile Enteritis. — Inquiry is necessary as to the mother's milk. If this is unsuitable, diluted cow's milk, one to two or three of barley water and lime water, ass's or goat's milk is advisable. Sterilised milk is often desirable; it is made by steaming it in bottles for half an hour before adding the lime water. If milk be rejected malt food is generally available; or raw beef juice, or Valentine's essence diluted freely, may be tried. Brandy is commonly of value, especially if any signs of collapse set in. The feeding-bottle must be kept scrupulously clean.

Ulcerative Colitis. — The feeding here is as for cases of dysentery or chronic diarrhœa. A drachm of fresh suet melted into a pint of warm milk is useful (the "Lac Sevi" of Guy's Hospital), and malted foods are available.

Typhlitis ; Perityphlitis. — Milk diet with lime water or sodium bicarbonate, whey, mutton essence. Any food likely to leave débris of tough or irritating matters must be avoided. If vomiting occur, the diet should be as recommended in cases of peritonitis.

Diarrhœa. — Milky diet, arrowroot and milk, a little raw arrowroot being stirred into each cupful. Mutton tea with rice; brandy or port wine with arrowroot. Sometimes equal parts, half an ounce each, of old port wine and good brandy, prove useful, taken two or three times a day when exhaustion occurs after severe vomiting and purging. No hot food is to be taken. When milk disagrees, veal or chicken broth, and malted

foods may prove of value. When arrowroot is not available, a few spoonfuls of flour, baked to a light brown pastry colour, may be given with water or milk.

Diarrhœa, as a symptom of tubercular enteritis, requires similar feeding, and the dietetic treatment of diarrhœa from whatever cause must generally be the same.

Constipation. — The diet should be varied, and should include vegetable food well cooked, especially spinach, fats, oil, fish or cooked fruits, brown bread, oatmeal porridge, whole meal bread, "parkin," gingerbread, and molasses. Cocoa is preferable to tea or coffee. Half a pint of cold water may be taken before breakfast, and the same at bedtime. Beef, white bread, cheese, and milk favour constipation.

Intestinal Obstruction. — The feeding in these cases is as for those of peritonitis. The less food given in any form the better. Nutrient enemata may be employed. Hot water in spoonfuls is useful, and whey. All food tending to leave curd or débris, as milk, is to be avoided.

Diseases of the Liver; Jaundice. — In cases of obstructive jaundice it is advisable to limit the amount of farinaceous and fatty foods. Beef and other animal foods and green vegetables are best. Milk and sodium bicarbonate with barley water is advisable. Water drinking is certainly of use. Alcohol should be avoided as a rule. However induced in any patient, the diet should be simple and unstimulating. Extra water drinking is often advisable, and Vichy water may be taken to the extent of fifteen or twenty ounces in the day.

Hepatic Dyspepsia; Lithæmia. — Plainly cooked animal food. Diminution of amylaceous food and fatty matters. Avoidance of seasoned and spiced food. Grilled mutton or beef, boiled white fish, spinach. Sugar in small amount and fruits. Claret or dry Moselle with water, or weak spirit and water, with meals, if desirable. Cold or hot water drinking is advisable between meals.

Cirrhosis of the Liver. — In this condition there is often gastro-enteric catarrh and vomiting of ingesta. Liquid nourishment in small quantities is necessary. Alcohol is to be withheld, as a rule, but it may be necessary to employ it for the patient even if contra-indicated for his disease. In many cases solid food may be given with advantage. If there be much ascites, restriction of fluids is advisable.

Cancer of the Liver. — The diet in these cases should be such as can best be digested. Saccharine and fatty matters are undesirable. A little alcohol is commonly of use, well diluted, or given in the form of champagne.

Gall-stones. — Saccharine and fatty matters are unadvisable. Mutton fat appears to favour formation of biliary calculi if taken to excess. Alcohol should be moderately employed, if at all; it is best given in the form of dry white Moselle wine with some sodic mineral water.

Peritonitis. — Vomiting and thirst are troublesome symptoms. Small pieces of ice to suck are useful, but no food should be given by the mouth. Hot water is sometimes well borne. Nutrient enemata are

to be given, consisting of milk, animal broth and yolk of egg, in quantities of not more than four ounces, every four or six hours. Nutrient suppositories are available. A little laudanum may be added to each enema. If the vomiting is in abeyance, alcohol may be given in iced water in small quantities. After abdominal section it is best to give no food by the mouth, and use small sips of hot water for twenty-four or thirty-six hours. Small nutrient enemata or suppositories may be given.

Chronic Peritonitis; Tubercular Peritonitis; Cancerous Peritonitis. — The diet must be adapted so as to avoid any articles difficult of digestion or likely to leave irritating débris behind them. Nourishing slop diet, pounded meats, arrowroot with cream, custards, mutton essence and jelly are available. Cocoa and malted foods are good.

Diseases of the Blood, Lymphatic System, and Ductless Glands. — *Anæmia; Chlorosis; Pernicious Anæmia.* — The dietary must vary in these cases according to the digestive capacity in each patient. The object is to supply abundance of nourishment in a readily digestible form. Red meat, milk, eggs, and fats are needed. The possible presence of associated gastric ulcer must be always borne in mind in young women, and appropriate feeding employed if there be even a suspicion of it. Wine is generally necessary, and four to six ounces of good Bordeaux or Burgundy may be given, or four ounces of port wine daily with food. In some cases marrow may be given with benefit, and this is well worthy of employment in cases of pernicious anæmia. The marrow from grilled ox-bones may be eaten with dry toast at one meal each day.

Leuchæmia. — Nourishing food is necessary in this disorder. Marrow is well worthy of trial. Some generous wine is also advisable.

Purpura. — Although there is no evidence to prove that this disorder in its ordinary forms is due to defect in diet, a simple nourishing dietary is always advisable, together with a plentiful supply of milk. Some wine is generally useful.

Scorbutus. — It is clearly proved that deprivation of fresh food, vegetable or animal, is the essential cause of this disease. It suffices to add this to a good nourishing diet to ensure complete recovery. Lemon juice is by itself sufficiently anti-scorbutic. The blood is deficient in alkalies. The gums being spongy and tender, and the teeth loosened in severe cases, it is necessary to employ spoon-food. Mashed potato, green vegetables, especially of the cruciferous variety, animal broths, softly-boiled onions, eggs, and fresh milk are then advisable. Red wines are of value. Freshly-made lemonade may be freely given. If vegetables are not available, fresh meat and blood prove of use in averting scurvy. In marine or other expeditions preserved vegetables and fruits should be provided. Vinegar is also useful. Lime juice should be served out daily in quantities of one ounce, and is generally mixed with 10 per cent of rum or other spirit to enable it to keep well.

Hæmophilia. — Great care is necessary to ensure that all food taken

is readily digestible. Fish should be given in place of excess of meat, and wine be sparingly employed, best in the form of diluted claret with meals. Note is to be taken of any periodic tendency to plethora. When hæmorrhages occur in the alimentary tract the diet should be that employed in cases of enteric fever with similar symptoms, whey and thin animal jellies only being given.

Myxœdema. — The modern treatment of this disease is carried out by supplying with the food thyroid elements in the form of various preparations of that gland taken from the sheep. This dosage must be maintained in perpetuity daily, or two or three times a week, in order to maintain immunity from recurrence of the disorder. Nourishing food and a little wine are of importance. Tablets or elixir of thyroid gland are best given after the principal meals, and the patient should remain sitting or recumbent for half an hour after the dose.

Addison's Disease. — Nourishing diet with wine is necessary. In exacerbations with vomiting and cardiac depression confinement to bed must be enjoined, and brandy in effervescing water or iced champagne and soda water be given. A small quantity of brandy or liqueur may advantageously be given after the two principal meals in the day. Oysters are often useful.

Hodgkin's Disease; Lymphadenoma. — In addition to a full nourishing diet, good results may be met with from the use of marrow, taken daily, as recommended in cases of pernicious anæmia.

Tuberculosis of Lymph Glands. — In these cases the diet is as for pulmonary phthisis. Fatty foods are of much value. Cream, suet and milk, malted food with cream or milk. Ass's and goat's milk, and whey, the latter charged with calcium chloride, twenty grains to the pint, are worthy of confidence.

Diseases of the Urinary Organs; Acute Tubal Nephritis. — It is now acknowledged that milk diet alone is desirable in this condition. Some skill is requisite to ensure its digestion, and to prevent aversion from it on the part of the patient. Fresh skimmed milk is best, diluted with one-third part of barley water. This may be alternated with whey. Draughts of distilled or Nieder-Selters water may be freely given. Only in mild forms, or when the kidneys begin to secrete actively, should farinaceous food be added. Arrowroot, rice, or well-made gruel may then be given. Next, bread and milk, sago, or rice and milk, bread and butter. Fresh lemonade, with a drachm of acid tartrate of potassium in each pint (imperial drink) may be given. No flesh food of any kind, or eggs, are to be employed in the acute disorder; as these are cautiously introduced, the effects on the urine must be noted daily. Any recurrence of hæmaturia at once contra-indicates flesh food. If vomiting occur it is well to cease administration of anything but iced soda water in small quantities.

Chronic Tubal Nephritis. — The diet best suited is that just advised for recovering stages of the acute form, great care being taken at first to watch the effect of animal (nitrogenised) foods on the amount of

albumin eliminated. Lemonade and green vegetables, as spinach, may be given if well cooked, also fresh fruits, potatoes, and saccharo-farinaceous elements. Fish is also available, and may be alternated with mutton or other tender meat. The patient, and not the disease, has to be treated, and too prolonged dietetic restrictions of a pedantic character may lead to wasting and a degree of low health incompatible with ultimate recovery. There are worse things than the mere loss of albumin.

Chronic Interstitial Nephritis. — The best diet in these cases is that compatible with the best health of the patient. The exact degree of adequacy of the kidneys must be gauged. Fish, vegetables, and farinaceous foods agree best. Animal food must be given in moderation, if at all; and red meat not more than once in the day. Alcohol is best avoided, or very sparingly allowed with one meal and well diluted. Any gouty element in a case must be appreciated. The high arterial pressure so commonly associated with granulating kidneys may be markedly reduced by diet alone, and a better level of health thus maintained.

Uræmia. — Milk and soda water or whey may be given. If vomiting is urgent, hot water may prove of use, and, after the bowels have been well cleared, enemata of milk (peptonised) may be given at regular intervals.

Lardaceous Disease of the Kidneys. — Milk diet is useful, and may also check tendency to a diarrhœa due to the lardaceous disease of the digestive mucous tract, which is commonly associated with that in the kidneys. In other respects the diet is as for chronic nephritis.

Renal Colic. — Warm diluent drinks are of use, unless vomiting is rebellious.

Morbid Urinary Conditions without Disease of the Kidneys. — *Diabetes Insipidus.* — The difficulty here is to meet the ardent thirst. Ordinary nourishing diet is to be given, and large amounts may be required as in saccharine diabetes. Fluids should not be freely taken with or immediately after meals. Some check to the craving for fluids may be secured by only permitting warm or slightly salt water to be drunk; but it is cruel and unavailing to limit materially the amount desired. Some Bordeaux or Burgundy wine may be given, also fresh lemonade.

Diabetes Mellitus; Glycosuria. — A very large clinical experience is needed in order to determine the dieting of any case of this disease. Every tiro in medicine knows what articles are theoretically prohibited for diabetic patients. For a fuller discussion I must refer to the article on Diabetes. The dietary may either be strict or partially so. It may need to be strict for a time, with subsequent and gradual relaxation, or, as in the case of chronic glycosuria which may or may not be a chronic form of diabetes mellitus, it may require but few or occasional restrictions. The strict diet precludes the taking of starchy and saccharine elements. This is a severe measure, and is hardly to be completely achieved or long endured. All varieties of animal food and white fish

are admissible is this case (with, perhaps, the exception of liver), fat in all forms, cream, milk sparingly, green vegetables, and sugarless wines and spirits. Bread stuffs can only be represented by gluten or almond bread or cakes. Tea, coffee, cocoa-nib decoction, and cocoa free from starch may be taken. In most cases this dietary causes disgust after a few weeks. Weight may be lost or gained in individual cases while submitting to it. If persisted in, patients of all classes may become demoralised, and take, by subterfuge, forbidden articles. Loss of sugar may in some cases be well borne, but the deprivation of bread, and the substitution for it of the sorry stuff, even in its best and costliest form, known as gluten "biscuits" and cakes, commonly intolerable after a time. Relaxation of rigid rules must then be permitted if we are to treat the patient and not merely his disease. Toasted stale bread, and bran bread made of the finest milled bran, may be given. Gluten bread as a cake may be soaked and toasted with plenty of butter, and so made more toothsome. Loosened teeth have to be reckoned with in severe cases. The appetite may be enormous, and no stint need be exercised either in solids or fluids. Dieting without medicinal treatment is, of course, in many cases insufficient, and in the worst forms the strictest diet is unavailing to check the disorder, even with associated medication. Each case is a study in itself.

Cases of glycosuria in obese persons of gouty proclivity calls for no rigid dieting, starchy food being taken in moderation, and sugar omitted. Biscuits, brown bread, toasted white bread can generally be taken, and potatoes occasionally in small quantities; rice, maccaroni, beans, and Jerusalem artichokes may be taken at intervals. Spinach is always advisable; sorrel, rhubarb, tomatoes, and fruits, fresh or preserved, and jams are all to be shunned. Dry Moselle wines and sound Bordeaux are the best forms of alcoholised fluids, or well-diluted spirits. Extra water drinking is commonly advisable, or Vichy, Nieder-Selters, Vals, St. Galmier water, or Saratoga water may be taken from time to time. A course of a dozen bottles in a month is very suitable in the case of Vichy (Celestins spring) or Vals water. Sweet courses may be replaced by light omelettes. Saccharin may be used to simulate the sweetness of sugar.

In all these cases regard is to be paid to the general health and well-being of the individual before us, and the bodily weight should be regularly ascertained at intervals.

Chronic Intoxications. — *Alcoholism; Delirium Tremens.* — The diet in these cases is as for chronic gastric catarrh. The patient is practically starved, and must be well fed by any available means. Nasal feeding may be necessary. Milk, strong soup, and coffee are useful. Peptonised foods may find a place here. Alcohol may or may not be required: there is no hard and fast rule respecting its use. A pint of porter or bitter beer may prove the best sedative or hypnotic in delirium tremens. If pneumonia occur stimulants may be freely needed, but the complication is

most grave. In chronic alcoholism, with gastric catarrh, all alcoholic liquids must be forbidden, and fluid nourishment be given till the appetite returns.

Lead Poisoning; Colic; Encephalopathia; Paralyses; Cachexia.—The diet must be regulated according to the special features in each case. Vomiting may be troublesome before colic supervenes, and may indicate uræmia in chronic cases with granular contraction of the kidneys. Milk and beef tea are best. In the chronic forms fatty food is very useful. The amount of nitrogenous food must be restricted if the kidneys are seriously inadequate to their functions.

Diseases of the Locomotory System. — *Rheumatic Fever.* — Without doubt the most satisfactory diet in this disease is that of milk and farinaceous matters. Milk and barley water, bread and milk, arrowroot, rice and milk, are the only allowable articles in the acute stage. Beef tea, animal broths, and nitrogenised foods are positively harmful, and prevent the most certain medicinal agents from acting efficiently. When all pain is subdued, and the temperature remains normal, remedial agents being still continued, possibly in diminished doses, mashed potato may be added to the diet; chicken broth, or tender white fish may be also carefully tried. Any return of pain or fever necessitates recourse to the earlier diet. Relapses are certainly induced by too early a return to animal food, however simple, and the employment of beef tea is particularly to be deprecated. Alcohol, as a rule, is best withheld, unless collapse and cardiac failure, as from pericarditis or myocarditis, occur. A relapse is practically certain if medicines be omitted and better diet be simultaneously prescribed. The return to ordinary diet should be very gradual.

Chronic Rheumatic Arthritis; Osteo-arthritis. — In pure cases of this disorder, which is in no sense rheumatic gout, the diet should be abundant and very nourishing; it may include meat, milk, fatty, farinaceous, and vegetable food, and alcohol or wine in any form. A full supply of cruciferous vegetables is advisable.

Gout, Acute and Chronic. — In acute gout, in young persons, a restricted diet is essential, and should consist for the most part of milk and farinaceous food. In older patients the diet may be more liberal, and include fish and green vegetables. Young persons may require no alcohol, older patients sometimes do better with diluted alcohol only at one or two meals in the day. There are many diversities of opinion as to the dietary of the gouty, both during acute attacks and in the intervals. Some physicians recommend animal food to be freely taken, and allow wine, others urge a contrary system. The fact is that there is no treatment for gout, but much for gouty patients. The age, antecedents, type of case, condition of organs and tissues, all require to be carefully considered in each. Farinaceous food in excess may be gout-provoking for some who do well on a moderate allowance of animal food. Some patients can take fruit or port wine with impunity, others suffer very soon from such a course. Without question the

majority do best on a moderate mixed diet of articles they can digest with comfort, care being taken to avoid excess in any one of them. Indulgence in the sweet courses, in rich dishes, in varieties of wine and malt liquor, in burnt fats and jams, and in large evening meals, is commonly gout-provoking. Any wines employed should be well matured and of good quality. Mature spirit and water is better than any wine when gout is threatening. The aged commonly require a little wine. Water drinking is certainly beneficial between meals. Fresh fats, starch and sugar have no direct influence on the production of uric acid. Caution is necessary in the use of meat, fowl, game and cheese. Bread, rice, green vegetables and fruit may generally be taken freely. Salt meats and salt should be used very sparingly by the gouty. Sherry, Madeira, Burgundy and Rhine wines are inadvisable. Champagne, of the best quality, and not less than six or eight years old, may be occasionally taken by many gouty persons. Dry Moselle and some Bordeaux wines are the least harmful, but of these the quantity taken should be moderate. Mature port wine may sometimes agree well, and not provoke gout, but the quantity is to be measured by a very few ounces. Diluted whisky or gin may generally be well borne, but should only be taken with food.

In subjects of gouty cachexia and tophaceous gout the diet should be as supporting as the adequacy of the kidneys will permit. Much harm may come in many gouty cases from withholding alcohol. Such a plan is occasionally imperative, but each case must be carefully considered by itself, and no routine practice is possible.

Gonorrhœal Synovitis. — After the severer pains have passed away it is necessary to give a good diet to these patients. The disorder is a lowering and depressing one, and the level of general health must be maintained as far as possible.

Rachitis. — The main treatment of rickets consists in improving the diet. Weaning is necessary, and cows', asses', or goats' milk substituted: this must be diluted according to the age of the patient, and lime water and cream may be added. Beef juice, chicken and veal broth, beef gravy, pounded mutton, yolk of egg are all advisable, and one or two meals of granulated malt, dissolved in milk are certainly valuable. Mashed potato, with milk or gravy, is useful. Condensed milk is most undesirable. Cod liver oil I regard as almost a part of the dietary.

Infantile Scurvy. — This disorder is practically a variety of rickets, with hæmorrhagic and scorbutic tendency superadded. The same diet is necessary here as for rickets, fresh milk and *purée* of potatoes being especially valuable. Orange or lemon juice, diluted and sweetened, and grapes may be given daily in small quantities.

Diseases of the Skin. — *Parasitic Diseases.* — In the varieties of parasitic skin diseases it is important to secure the highest general nutrition. In ringworm it is found advantageous to employ milk and fatty food freely, and a thoroughly good digestible diet.

Erythemata. — A rheumatic element is often present in many of these manifestations, but it can hardly be specifically reached by dietetic measures. Chilblains attack persons of this habit, and those of gouty inheritance, with some frequency. A good diet, with some wine, is often helpful in preventing their occurrence.

Urticaria. — The diet should be plain, and personal idiosyncrasies should be noted as to the influence of fruit, honey, shell-fish, or certain wines.

Eczema. — Much benefit is to be derived from precautions in diet in many varieties of eczema. Condiments should be dispensed with altogether, or as far as possible. Sugar and salt are sometimes provocative, and highly-seasoned, salted, and concentrated foods, and even ham and bacon should be avoided. Vinegar and even fresh fruits are sometimes harmful. Tomatoes, sorrel and rhubarb are inadvisable. Soups are not seldom to be placed in the same category. A gouty tendency is often expressed in eczema, and the dietetic management for the former is commonly effectual in disposing of outbursts of the latter. In acute diffused eczema the diet should be that suitable for a febrile condition.

Pityriasis rubra; Exfoliative Dermatitis. — Good diet is certainly helpful in many of these cases. The general level of nutrition is commonly low.

Psoriasis. — The diet in these cases should be that recommended for eczema. Thyroid feeding has certainly proved of benefit in some cases, and may be tried.

Acne vulgaris; Gutta rosacea. — Some variety of dyspepsia is commonly associated with these disorders. Plain food, with avoidance of alcohol, seasoned and hard meats, coffee, cheese, pickles, and much fat is advisable.

Lupus. — The tubercular nature of this disorder naturally suggests a diet which is suitable for those so disposed. Of late some good results have been obtained by thyroid feeding as for myxœdema.

Boils; Carbuncles. — The most satisfactory diet when these disorders are in progress is a milky-farinaceous one, without stimulant. If there is obvious debility an ordinary good diet is necessary, and wine may be given. Otherwise it is better to reserve the use of wine till the sloughs are separating. One or two ounces of fresh yeast (brewer's barm), taken several times in the day, has been found of use where successions of boils are in progress. It is important to recognise any associated gouty or glycosuric condition in these cases, and of course to modify the diet accordingly.

Atrophy. — The dietetic treatment of this condition must vary with the essential cause of it in every case. Some degree or variety of dyspepsia is often a cause, and inability to take appropriate nutriment is also often an underlying condition. Digestive incapacity for starch and milky food may have to be overcome, and effort is to be made to give a fair proportion of these with fatty and albuminoid stuff. Oatmeal gruel,

malted food, with milk, yolk of egg, oysters, tender meats, game, fat ham, cream, butter, cocoa, and porter are all of service if they can be digested. Half an ounce of rum in half a pint of warm new milk may be given before leaving bed each morning, and a fat mutton chop, with half a pint of draught porter, constitutes an appropriate luncheon. Custard pudding with Devonshire cream, or suet and milk (a drachm of fresh beef suet dissolved in half a pint of hot milk), are worthy of trial.

In the foregoing article I have endeavoured to set before the reader the general principles relating to clinical dietetics as adapted for patients suffering from various morbid conditions. It will be understood that nothing herein recommended can ever replace the necessary and associated medicinal and other means which are requisite in order to favour restoration to health. Diet may, and can do much in this direction, but the clinical practitioner must conduct as well the dietetic as the other therapeutical measures in each case, and if he fail at the same time to *manage* his patient, neither the one nor the other will avail him to promote the sole object of his art, which is to ensure the recovery of the sick. DYCE DUCKWORTH.

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D. D.

THE DIET AND THERAPEUTICS OF CHILDREN

ALTHOUGH on account of his special constitutional peculiarities the young child bears but a faint resemblance to the fully developed adult, in one respect the likeness is close enough. It is that young children, like their elders, differ curiously amongst themselves not only in general digestive capacity, but also in their individual ability to assimilate this or that kind of food. One baby thrives upon fare which is innutritious if not actively hurtful to another; so that to prescribe a dietary for a

young infant is to engage in an experiment which, if it do not succeed at once, may require many changes in detail before it can be brought to a successful issue.

So long as the infant can be fed from the breast all is likely to go well; for in human milk he meets with a digestible and amply nutritious fluid which he swallows straight from the gland, pure and uncontaminated by germs. There are few children who do not thrive when thus fed, provided, of course, that the supply of milk be sufficient and its quality good. But so many mothers are unable to nurse their babies that a large proportion of infants have to be brought up by other means. The problem is to imitate the natural food of which the child has been deprived. The more closely this can be done the better the prospect of rearing the infant with success.

To be accurately adapted to the wants of the infant, the required food must contain all the elements of nutrition as nearly as possible in the proportions observed in human milk; it must be well within the powers of the stomach, so as to leave little undigested residue to ferment in the bowels and be a source of mischief; it must be fresh and in good condition; and, lastly, to be a perfect food, it should contain a sufficient proportion of the vitalising element — whatever that may be — which endows it with its antiscorbutic properties. Now milk contains in itself all the elements of nutrition; and the milk of many animals approaches human milk in composition more or less closely. Any of these may be used; but practically we are forced for convenience' sake to fall back upon cow's milk, which is always at hand; and this can be adapted to our purpose without much difficulty.

As compared with human milk,[1] the milk of the cow contains a larger proportion of curd, but is deficient in sugar and to a small extent in fat. To bring it, then, to the standard of human milk it must be diluted and sweetened. But this is not enough. The curd of cow's milk coagulates in one large, tough lump which resists digestion; while that from the human breast forms a light, loose clot which is easily penetrated by the digestive fluids. When, therefore, cow's milk is used, steps must be taken to prevent this firm clotting of the curd. If we add to the milk some thickening material the particles of curd are kept apart, so that when the casein coagulates in the infant's stomach by the action of the gastric juice the clot consists, primarily at any rate, of a multitude of little lumps of curd instead of one solid mass. For the thickening material some form of starch is often used; but as this is difficult of digestion by the young child, barley water is to be preferred. Barley water itself contains starch, but in comparatively small quantity and very finely divided. It rarely disagrees, and when mixed with a fourth part of milk suits the large majority of new-born infants. The

[1] For purposes of comparison Dr. V. A. Meigs' (1) analysis is subjoined: —

	Water.	Sugar.	Casein.	Fat.	Ash.
Woman's milk	87·163	7·407	1·046	4·283	·101
Cow's milk	88·549	4·898	2·792	3·310	·451

meal should be sweetened with white sugar; and it is important that the barley water should be freshly made, for it cannot be given with safety if more than six hours old. If the cow's milk be used uncooked as it is delivered to the house, it retains all its antiscorbutic properties: on the other hand, in this state it is probably loaded with germs of various kinds, which may indeed be harmless, but may be capable of exciting dangerous fermentations, or conveying the seeds of serious disease. Epidemics of diphtheria and scarlatina, as well as bowel complaints of great gravity, may owe their origin to impure milk. Unfortunately boiling the milk renders it less active as an antiscorbutic; but it is wiser to make this sacrifice for the sake of avoiding the greater evil, and to use milk which has been boiled or sterilised. If the latter, it is best to add the barley water to the milk before sterilisation,[1] and to allow the child to suck the mixture from the sterilising bottle fitted with a mouthpiece.

This method of feeding is to be preferred to the common plan of giving milk and water alkalised with a third part of lime water. The lime water acts by partially neutralising the gastric juice, so that a considerable proportion of the milk passes uncoagulated from the stomach and is digested in the bowels. Healthy babies doubtless often thrive upon this food, although thus deprived of a very important agent of digestion.

It may happen that the new-born infant has a special inability to digest fresh cow's milk. In that case he will often do well for the first few months upon condensed milk and water; but cow's milk sterilised and thickened with barley water should be tried again after an interval, varying the proportion of milk in the mixture to suit the child's digestive capabilities, for an infant who is greatly overtasked by a third part of milk may digest a sixth with ease. No effort should be spared to enable the child to digest the fresh milk, for condensed milk is a very undesirable food for him after he is three months old. In all cases of difficulty, cow's milk peptonised in the house should be tried, and will often agree. We should also never fail to inquire as to the cleanliness of the feeding-bottle and the times of feeding. Much may often be done by careful regulation of these matters.

The temperature of the meal should be 95°, and the food can be easily warmed to this heat by placing the bottle in a small basin filled with hot water. The quantity given in the first week should be a couple of ounces, but more will very soon be required. The regulation of quantity is a matter of small importance. If a proper interval be allowed for digestion the quantity taken at each meal may be left safely to the child himself. A very young baby can be trusted to stop sucking when he has had enough, and any excess which may have been swallowed is usually regurgitated without effort shortly after the meal.

Children may do well for the first six months upon milk and barley

[1] Milk sterilised in the house by Soxhtet's apparatus is greatly to be preferred to that supplied by a company.

water alone without any change; but often they require more variety in their food: in all cases where the digestion is difficult, and has to be humoured, variety in the diet is too important a stimulus to be neglected. Sooner or later, then, the question of "Infant's Foods" has to be considered. All these are preserved or tinned foods, and therefore destitute of antiscorbutic properties. On this account they are only allowable as aids in the diet, for cow's milk, when this can be borne, must always be our mainstay.

The tinned foods may be divided into four classes, viz., —

1. Milk concentrated by evaporation to the consistence of thick cream and preserved with sugar or malt.

2. Milk desiccated and mixed with partially converted starch.

3. Foods consisting of wheaten flour more or less completely digested, or mixed with malt or pancreatine.

4. Foods consisting merely of the flour of some cereal baked.

All these, as foods, leave something to be desired; for besides that none of them possesses antiscorbutic properties, all are found in some respects to be faulty as nutritives. According to the analyses of Dr. A. Stutzer (2), of Bonn, most are lacking in fat; and in many the amount of protein is too small and its proportion to the other nutritious matters too narrow. Some are weak in bone forming material; others contain insoluble carbohydrates (unconverted starch) in excessive quantity, and therefore trying to the digestive capacities of an infant. But although beneath the standard of perfect nutrients, and ill fitted to be for long together the sole nourishment of a young child, these foods are by no means useless. As additions to the cow's milk, providing supplementary nourishment, furnishing material for flattering the palate and giving variety and relish to the meals, their value is great. For infants who cannot digest fresh cow's milk we find in the foods containing desiccated and condensed milk a fair temporary substitute; and even if the inability prove permanent, we can often by this means and a little management maintain the child in a fair state of nutrition until he is of an age to supply the deficiencies of his dietary by other means.

The choice of the food is of great importance. Class I., which contains the syrupy condensed milks, should be reserved for the first three months of life. Dr. Rotch (3) advises that these milks be diluted with nine parts of water, and that 20 per cent of cream be added to supply the deficiency in the fat. This should be about a teaspoonful of cream to the bottle of food. The only other tinned food allowable at this age is Mellin's Food, which belongs to Class III. In this the starch is almost completely predigested and converted into dextrine and maltose. One or two teaspoonfuls may be added to each alternate meal of milk and barley water for the sake of giving variety. Starches are to be used for infants below the age of six months with great caution. The secretion of saliva is very small for some time after birth, and does not become free until the third month; and the pancreatic secretion is very scanty for the first six months of life, and does not acquire its full

diastasic action for some months longer. Up to the age of six months starch should only be given when guarded with a digestive, as in the malted foods or Benger's pancreatic food. Later it may be tried cautiously and in small quantity without this safeguard, in the form of baked flour or a rusk, but always with milk. Any of the foods in Class IV. may be used at this time.

The child should be fed every two hours for the first six weeks; then the interval between the meals can be gradually increased, and the meals themselves made larger and more satisfying. When a tinned preparation is used it must not be added to the milk until the meal time comes round, for if the food be allowed to stand ready made it quickly begins to ferment.

It would be out of place here to refer to the various derangements which may affect the hand-fed infant, or the changes in the diet which such disorders require. The reader should consult special treatises for information upon these important points. It will be sufficient to state, as a general rule, that whenever digestion is difficult and the nutrition of the child unsatisfactory we should aim at plenty of variety in his meals; that we should not persevere with a food which is found not to agree; and that as cooked milk is weak in antiscorbutic properties we must be always on the watch, while using it, for early signs of infantile scurvy. It may also be remarked that healthy digestion depends in a great measure upon the general management of the infant. Soiled linen should be removed from the nursery without delay, and the room should be frequently ventilated so as to keep the air fairly pure. Great attention, too, should be paid to warmth of the child's feet and legs; and the washing of his body should be carried out as quickly as possible and without undue exposure. An infant whose feet are habitually cold never has a good digestion; and many a fatal attack of gastritis has owed its origin to a chill contracted by careless exposure in or after the daily bath.

At the end of the first twelve months the infant may be allowed for his dinner some weak veal or chicken broth thickened with barley and strained. On alternate days he may take the yolk of a new-laid egg lightly boiled or beaten up with milk. At this time it is advisable to accustom the child to take food from a cup or spoon, so as gradually to wean him from the bottle; and when he enters upon his second year a light pudding made from sponge cake or rusk may be given two or three times a week.

Meat must not be allowed until the child is sixteen months old: he may then begin to take a little underdone mutton chop. At first this should be pounded in a mortar and rubbed through a wire sieve; but after a month or so it will be sufficient to mince it very finely. It is important that all changes made in the diet be made cautiously and with judgment. A time should be chosen when the child is happy and cheerful, digesting without trouble and sleeping quietly, and the new food must be given in small quantity at first. A change made when the

child is teething or fretful or restless at night is hardly likely to be attended with success. At first meat should be given twice a week only. On other days the dinner should consist of strong soup with some well-boiled vegetable, such as cauliflower, vegetable marrow, or tender French beans. Once or twice a week the child may take some chicken or boiled fish. Potatoes are not to be allowed every day; and batter pudding, and puddings made from bread and rusk, are to be preferred, as less purely farinaceous, to rice, sago, and tapioca; although the latter are, no doubt, sanctioned by nursery tradition and prejudice. But an excess of starch in their diet is to be avoided for growing boys and girls. At no time of life do young children find the digestion of starch an easy matter; and it is unwise to overload them with a food which fattens but gives little strength, and is but too apt to make them lethargic and dull. Beef and mutton, as a rule, they can digest without difficulty. I have been told many times that this child or that could digest no meat, but have always found that it was not the meat, but the potato eaten with it which disagreed. Cold meat, again, is as harmless as hot; and minces and hashes are not to be withheld from children through any groundless fear of "twice cooked" meat. Nursery superstitions, like other delusions, die hard; but dishes in which the meat is merely warmed through without being really cooked a second time are innocent enough. At all ages variety in diet is to be aimed at; and ham and tongue (thinly sliced) and bacon for breakfast, help to lighten the monotony of the daily meals and stimulate the digestion as well as gratify the palate.

A word may be said as to the arrangement of the meals. Arbitrary custom ordains that the two substantial meals of the day — the breakfast and dinner — must be confined to six hours out of the twenty-four; and that for the remaining eighteen hours the child must take nothing but milk and bread and butter, with the addition, perhaps, of cake or a little jam. This arrangement answers fairly well with sturdy subjects who can be prepared with an appetite at the prescribed times, although even with these a more rational distribution of their food is to be preferred. But many children, especially those who are anæmic and fragile, cannot thus be hungry at command. Often in the forenoon they do not care to eat at all. They hardly touch breakfast, and only trifle with the mid-day dinner. Towards evening, however, the appetite improves, and at five or six o'clock they would eat a hearty meal if allowed to do so. For years in these cases I have adopted the plan of ordering a substantial meal towards the end of the day, at the time when the child is best disposed to take it; and if the more fermentable articles, such as sweets and potatoes, be excluded from the menu, and a good hour before bedtime be allowed for digestion, I have rarely found the patient anything but the better for the change. In these cases a little stimulant is often a help in improving the appetite and aiding digestion. It should be given with the principal meal. I often order the St. Raphael wine, but any sound wine will usually agree provided it be not acid. I think a good Burgundy is to be preferred to a claret. Alcohol must be regarded strictly as a

medicine in the case of a child, and is not to be ordered except to serve a temporary purpose. It has no tonic properties, and must be discontinued when the appetite improves.

Diet enters so largely into the treatment of children's diseases, and the rate of recovery may be so influenced by a judicious selection of the food, that an intimate acquaintance with these matters is indispensable to success as a practical therapeutist. Children, especially young children, are more dependent than adults upon a daily supply of nourishment, and suffer more in proportion if this be withheld. The digestion fluctuates from day to day in strict relation to the general health; and flags at once when this is impaired. In acute disease with a high temperature the digestive power is very limited, and in order that the nutritive supply be not cut off altogether, the food provided must be of the lightest and most digestible kind. But "light" food is not to be taken to mean farinaceous food. Starches, especially when cooked with milk, are ill-suited to such a condition, and must be given, if given at all, with great caution, or they may do harm. As a thickening material for broth they are more useful, and beef tea thickened with tapioca or arrowroot will often agree when a common tapioca pudding only excites discomfort from acidity and flatulence. It is important to realise early that rice and sago and such-like puddings are not "light" or easily digestible foods; and that to task a disordered or weakened stomach with such highly fermentable material in a case of acute illness, or during an early stage of convalescence from grave disease, is to aggravate the symptoms and seriously retard recovery. In the dieting of febrile diseases in the child the rules which regulate the hand-feeding of infants should be observed. Starch should not be given with milk unless guarded by a digestive; and milk itself, if not peptonised, must be thickened with barley water or gelatine. The meat jellies and cold extracts of meat agree well with children beyond the age of infancy, if not given too liberally. The quantity allowed in each case is to be determined by the strength of the child and the state of his stomach. A rise of temperature, disturbed sleep, or discomfort after the meal, may be taken to show that the quantity must be reduced. So, also, if during convalescence the urine be habitually thick with lithates it is usually a sign that the patient is being overfed.

It is often curious to note the immediate improvement which takes place in the condition of a sick child when an excessive dietary is reduced, and the food both in quantity and quality is adapted with judgment to the enfeebled powers of the patient. But it is not enough to see that nourishment is assimilated with little effort; we have also to take care that waste products are freely eliminated; that the bodily heat, if excessive, is controlled; and that the skin, the kidneys, and the bowels are encouraged to the full discharge of their duties. Moreover, we must be careful to enforce proper rest, and to have the air of the room maintained at a suitable temperature and frequently renewed.

The constitutional peculiarities of the young child have an important bearing upon the treatment of disease in early life. The curious sensitive-

ness of the nervous system gives an especial value to counter-irritants of the skin and external applications generally. Amongst these remedies baths take the first place. The hot bath (100° F.) is an important general stimulant in cases of extreme depression either from hæmorrhage, profuse diarrhœa, vomiting, pulmonary collapse, severe nervous shock, or any other depressing agency. When used with this object, the child must not remain longer than three or four minutes in the hot water. This bath can be made more stimulating by the addition of flour of mustard in the proportion of one ounce to each gallon of water. The mustard is first mixed into a paste with cold water, and is then squeezed through a piece of fine muslin into the bath.

The warm bath (90° F.) calms excitement, allays spasm, and induces sleep. It is useful in cases of reflex convulsions and every form of nervous agitation. Its diaphoretic action makes it of great service in Bright's disease, especially if the child be afterwards wrapped in blankets to keep up the action of the skin. The duration of the warm bath should be from fifteen to twenty minutes.

The cold douche (65°–70° F.) is only useful in the morning before breakfast. If given rapidly it is a bracing tonic for children in whom the system responds readily to the shock. Even pallid, delicate subjects derive great benefit from it if proper precautions be taken to promote a healthy reaction. In the case of a weakly child the patient should be first rapidly sponged in a hot bath (100°), and should receive the douche as he sits in the hot water. Immediately afterwards he should be wrapped up undried in a hot blanket, and returned for a few minutes to his bed. Reaction is hastened if the child drink a cup of hot milk ten minutes before being put into the water. This is the only way in which cold or nearly cold water can be used to advantage with children whose nutrition is at fault. The cold sponging so often employed is highly objectionable for such patients on account of the long exposure it involves. Even when the douche is used as described above, its temperature must be carefully adjusted to the readiness of reaction shown by the patient. Some children respond best to a comparatively low temperature, while others, whose power of reaction is slight, require a douche of 75° or even 80°, and are depressed instead of strengthened if the water be colder.

There is another method of using water externally, which is sometimes of the highest value. In cases of ptomaine poisoning, with or without vomiting or diarrhœa, the skin loses its elasticity more or less completely, so that when pinched up it lies in loose folds upon the abdomen. This state of skin is probably a sign of imperfect action of the kidneys, for the urinary secretion at the time is almost invariably scanty, and is sometimes suppressed. At any rate, unless the elasticity of the skin can be restored the patient will almost certainly die. It is my custom in these cases to pack the child in a large towel wrung out of cold water, or of water containing a sixth part of eau de Cologne or brandy, and to keep him well covered and packed in with many blankets for hours together. At the end of every three hours the child is unswathed, rubbed dry, and

repacked as before. After some hours of this treatment the kidneys begin to act more freely and the skin to recover its elasticity. I have kept young children, thus packed, for twenty-four hours together with the very best results; for if by this means the elasticity of the skin return, the prospects of the child's recovery are very materially improved. This form of blanket bath should be reserved for cases where it is desired to increase the action of the skin or kidneys. It cannot be relied upon to lower the temperature when this is high; for unless the process set up copious perspiration, the heat of the blankets increases the pyrexia instead of lessening it. Children as a rule bear high temperatures well; but if the bodily heat exceed 105° steps must be taken to reduce it. The plan I prefer consists in wrapping the patient in a sheet wrung out of cold water, and covering merely with another dry sheet. Under this treatment the temperature quickly falls; and if the pyrexia have been accompanied by convulsions or great excitement, the nervous disturbance, as a rule, quickly subsides, and the child sinks into a quiet sleep.

Of the baths above described the hot and mustard baths may be considered as counter-irritants and general stimulants. Children respond well to counter-irritation, whether this be used generally or locally. In cases of bronchitis or catarrhal pneumonia, long-continued counter-irritation with mustard poultices diluted with four or five times the quantity of linseed meal, and thoroughly mixed, is of the utmost service. A large weak poultice kept on the skin for six or eight hours is to be preferred, as a rule, to a stronger application used for a shorter period; but in cases of imminent danger, where an immediate effect is required, a mustard leaf or even dry cupping of the back will often produce speedy relief. Mustard leaves, however, and violent applications such as blisters, are not to be recommended in the case of babies and the younger children, and must be used with caution even with older subjects who are cachectic or ill-nourished; for troublesome ulcerations or even gangrene of the skin are occasionally seen to follow their use. Moreover, it must be remembered that a blister is equal to a burn of the third degree, and may have a seriously exhausting effect upon a weakly child. In a properly selected case, however, the value of this form of counter-irritation is great. In peri- and endo-carditis no time should be lost in having recourse to it. I believe I have often succeeded in cutting short an attack of pericarditis by a timely blister; and the value of a vesicant in promoting absorption when the pericardial sac is full of fluid admits of no reasonable doubt. In such a case, when used to a young child, the blister must be of small size, and must be kept in contact with the skin for a short time only. Thus it can be applied for two hours to a child of three years old, and half an hour longer for each additional year of life. If the blister have not formed when the irritant is removed, a bread and water poultice will soon cause it to rise up. In cases of exceptional delicacy of skin a sheet of oiled tissue paper may be interposed between the blister and the surface to be acted on, as recommended by Bretonneau.

Frictions of the skin with almond oil or stimulating liniments are

useful in various conditions. Threatened collapse of the lung may often be averted by this means; and if atelectasis have occurred, persevering friction with strong counter-irritants may do much in helping the lung to re-expand. In whooping-cough the use of rubefacient embrocations is held in high esteem as a domestic remedy; and in all cases of chronic disease friction of the surface combined with systematic massage of the muscles has a general as well as a local value. In chronic digestive derangements the skin is often dry, scaly, and inactive. For this condition the application of warm almond oil becomes a useful resource. The patient is first well sponged in a bath of hot soap-suds, then quickly dried, and freely anointed all over the body with the warm oil. He is then put to bed in a flannel night-dress or wrapped in a blanket. The efficacy of a few repetitions of this treatment in improving nutrition and making the skin soft and supple is remarkable.

Children are very easily depressed by acute disease, so that it is important to watch for early signs of failure. On this account alcoholic stimulants take a high place among internal remedies, and a few doses of this medicine will often in a few hours completely alter the aspect of a case, and turn the scale in favour of recovery. In chronic disease, also, the effect is equally beneficial. It is a matter of common observation at the East London Hospital for Children, that the young patients who are enfeebled and wasted by privations of all kinds, combined with long-continued ill-health, often make no response to the action of drugs until their exhausted energies have been revived by a few doses of wine or brandy.

The rapidity with which nutrition suffers in early life, when any hindrance arises to the easy assimilation of food, gives great value to all invigorating remedies. But tonics are not to be ordered indiscriminately. It is of small use to prescribe iron or the mineral acids for a sickly-looking child merely because he is anæmic and weakly, and leave unnoticed a chronic gastric derangement which is the cause of his poor appetite and feeble digestion. The dyspepsia must first be treated with alkalies and stomachics, and by a judicious limitation of the more fermentable articles of food, before tonics can be given with any good result. As the digestion is liable to suffer in all the ailments of childhood the alkalies are perhaps the most useful of our remedies. By this means we check the excessive secretion of mucus and neutralise acidity. Moreover, the addition of an antiseptic, such as spirits of chloroform, and of warming aromatics, arrests fermentation and reduces flatulence. At this period of life, whenever alkaline remedies are prescribed, an aromatic, such as cinnamon, dill, or peppermint, should always be included in the mixture.

When tonics are given the dilute nitro-muriatic acid is very useful with small doses of nux vomica; and children take quinine with great benefit if the dose be not too small. After any of the infectious fevers quinine is always indicated. A child of twelve months old will take a grain three times a day; and half a grain may be added for each year of the child's life until a dose of three grains is reached. This can be given three, four, or six times in the day as may seem desirable. The usual

doses ordered for children are too small; for young patients are not at all susceptible to the alkaloid, and rarely suffer from cinchonism. Cod liver oil is the favourite remedy for every form of wasting or pallor. The oil is only useful when the digestion is in fair order, and should never be given to a bilious or dyspeptic child. It is usually administered in quantities far too large. A child of twelve months old can rarely digest more than ten drops at one time, and a teaspoonful should be the maximum dose at any age.

The dosage of medicine for children is often a cause of some perplexity. Of certain drugs they show a curious tolerance. Belladonna they can take in large doses, for although a few drops of the tincture may bring out the characteristic rash, this is not a symptom of excess, and has no relation to the size of the dose. To opium, as is well known, they are keenly susceptible. It is wise to prescribe this narcotic in very small quantities, but to repeat the dose as frequently as may be necessary. If this be done, and we give directions that the child is never to be waked up to take his medicine, we need have no fear of his becoming narcotised. In connection with this subject it may be remarked, that infants who are being drugged by unscrupulous nurses with "soothing syrups," or other opiates, invariably show it by symptoms which are characteristic enough to the experienced eye. The child lies in a drowsy state with contracted pupils, he often vomits, his bowels are obstinately confined, his water is scanty, and his skin is curiously inelastic. If this combination of symptoms be noticed in a young baby we have the strongest reasons for suspecting the secret administration of a narcotic.

Antipyrin, like quinine, children take well; and arsenic and iodide of potassium may be given to patients of four years old and upwards in the doses usually prescribed for the adult. Ergot, digitalis and lobelia are other remedies which may be ordered with a liberal hand. The making of these and other drugs palatable to young children is far from easy. The bitterness of quinine it is impossible to disguise completely; but it may be modified by giving it suspended in glycerine and water. Nauseous powders are best given in "cachets"; and young children soon learn to swallow them. It is wise to avoid the use of syrups for sweetening purposes: there are few illnesses in young people which are not complicated by a certain amount of gastric disturbance; and the quantity of sugar contained in the syrups must provide additional material for fermentation, and excite acidity and flatulence. There is no doubt that the medicated syrups, which are manufactured so largely, are often the cause of great discomfort to the patient, if not of worse evils; the syrup, by increasing the digestive derangement, may be more productive of ill than the drug dissolved in it is of good.

EUSTACE SMITH.

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E. S.

NURSING[1]

Tending the sick has risen to the dignity of a profession, and a special training is required for those who undertake it. The keynote of good nursing is an intelligent obedience, only attainable by systematic education. Women who wish to be nurses need practical skill, powers of observation, and tact in dealing with various idiosyncrasies. They must also remember that time is needed in which to gain these qualities and the knowledge which experience alone can give.

Hospitals, which offer facilities for regular instruction both in theory and practice, have become training schools for nurses. Order, method, punctuality, obedience are part of the groundwork of a training school; but to these must be added thoroughness, promptness, accuracy in observing and correctness in reporting observations, and a loyal attitude towards doctors and patients. The whole art of trained nursing depends upon the maintenance of this attitude. Nurses are bound, by their very position, to render loyal obedience to medical men. It is not their duty to suggest or initiate treatment of any kind, except by express permission or in some sudden emergency. They have no responsibility whatever save that of faithfully obeying orders, and the higher the discipline the more readily this is recognised.

With regard to patients the gravest fault, short of negligence, is love of gossip, personal or professional. To talk to patients about their ailments and treatment, to describe other cases to them, to indulge them in medical histories, and to discuss the comparative merits of medical men, work infinite harm; especially to those of nervous temperament who are chiefly disposed to seek such confidences. It is true a nurse is often at a loss to interest her patients, but to gratify unwholesome curiosity, to criticise methods of treatment, or to reveal private affairs learned in the course of her profession, is most reprehensible.

Age for Training. — While probationers are being thus educated they are also instructed in the special branches of the work. The demands upon physical power and mental assimilation are alike heavy, and should not be undertaken too soon in life. From 23 to 24 is the earliest age at which a nurse should begin her training. Even in children's hospitals to accept younger probationers is an error. The actual strain of lifting, moving, etc., may not be so heavy; but the incessant watchfulness, cheerfulness, and absolute self-control necessary in dealing with children are a heavier task than is usually supposed.

General hospital training may be divided into surgical and medical work, and the probationers are moved from ward to ward at the discretion of those in charge of the training. For the sake of order and dis-

[1] I have asked Miss Hughes to write this article for me in order that medical men may know what to expect of their nurses — not that I for a moment suppose any one of my readers to be unfamiliar with the smallest of these bedside services. — Ed.

cipline this power should be vested in the matron, herself a trained nurse, who is guided by the reports of the "sisters" or "charge nurses" of the different wards.

Surgical Ward Work; Ventilation. — The first essential in a surgical ward is pure air, the second absolute cleanliness. On the nurse devolves the management of windows and ventilators so as to obtain the maximum of change of air with the minimum of draught. Common sense must be brought to bear on the matter; the direction of the wind and its effect on the ventilating arrangements of the ward must be considered, so as to avoid a through draught, also the nature of the warming apparatus, whether open fireplaces or hot pipes, and its position in regard to doors and windows. The usual temperature — from 50° F. to 60° F. — should be recorded at regular intervals during the twenty-four hours, and freshness must be equally maintained day and night.

Absolute cleanliness applies to every detail of a ward, from the patients and their beds to the smallest appliance and fitting. Dusting means not merely moving the offending material, but removing it from every part of the walls, floor, furniture, etc. A damp, not wet duster is most effectual; and if desired, it can be used with a disinfectant. Floors should be sprinkled before sweeping, and the bedstead of every patient dusted daily.

Every appliance must be scrupulously cleansed, no stains nor fur allowed on utensils, test tubes, etc.; strong soda water, or spirits of salt (applied with a mop) will cleanse any glass or earthenware vessel, but the latter must not be used for metals, nor for lavatories, on account of the metal fittings. Bedsteads, bedding, mackintoshes, splints, etc., must be kept absolutely clean.

Surgical cleanliness is a higher matter than general cleanliness. It aims at the destruction of every germ; bacteria are not merely to be removed, they should be non-existent.

This is attained by boiling all glass and metal appliances for twenty minutes, maintaining the temperature at 212° F. Dressings, sponges, wool pads, are also sterilised, and kept hermetically sealed till the moment they are needed. Other antiseptic dressings, such as sal-alembroth, cyanide, etc., have the same object in view; and here the most careful watchfulness is demanded from the nurse that she shall not nullify the treatment by any such careless action as laying down a dressing, scissors, or any of the appliances, on an undisinfected surface. She must herself be scrupulously clean in person and dress, and her hands must be carefully kept, with short clean nails.

Cleansing of Hands. — In attending upon the surgeon, or in preparing for dressing cases, etc., her hands may be rendered free from suspicion by first thoroughly washing in hot water, using carbolic soap and nail brush freely; hands and forearms are then immersed in strong Condy's fluid for a minute, the stains being next removed by the use of a saturated solution of oxalic acid. After drying, they are again soaked in $\frac{1}{500}$ solution of perchloride of mercury, and may then be considered as really

cleansed. This process does not take long, and is especially necessary in moving from any doubtful case to another patient.

A knowledge of the various **strengths of disinfectant and antiseptic lotions** is important to the nurse.

(*a*) *Perchloride of Mercury* is used $\frac{1}{5000}$ for hands, $\frac{1}{4000}$ for douches, etc., other strengths being specially ordered. Metal instruments should be wiped at once if immersed in it.

(*b*) *Carbolic acid* lotion is used $\frac{1}{20}$ for hands, instruments, and external washing of sound skin, $\frac{1}{40}$ and $\frac{1}{60}$ for wounds, etc.

(*c*) *Condy's Fluid*, ʒj. to Oj. (or three to four crystals of permanganate of potash to 1 pint) for douches, wounds, etc.; it stains linen, instruments, and hands.

(*d*) *Saturated solution of Boracic acid*, $\frac{1}{26}$ or about 4 per cent for wounds.

(*e*) *Sanitas*, ʒj. to Oj., a pleasant deodorant for foul wounds, and for cancer, gangrene, etc.

(*f*) *Creolin*, ʒj. to Oj. for hands and instruments; must be mixed with a little cold water before adding hot, and can be used with soap. Same strength useful for irrigating wounds.

(*g*) *Boiling water* for instruments. *Boiled* water for douches and irrigations.

Poison Bottles and Lotions. — Every poisonous lotion should be in a special bottle, with conspicuous label, and kept under lock and key; any possibility of confusion with medicines, or beverages, whether in or out of use, should be prevented. Corrosive sublimate is usually coloured pink or blue to avoid mistakes; the other lotions, except boracic lotion, have each a distinctive and easily perceptible smell.

Symptoms of their absorption must be looked for and reported, *e.g.* in carbolic poisoning, dark green urine, drowsiness, muscular weakness, and sometimes vomiting.

If a nurse has **dressings** to prepare for granulating wounds, the lint or gauze must be cut exactly to cover the sore to avoid softening the edges.

Ointments must be very thinly spread, and must never be allowed to accumulate on the sound skin. If a moist dressing is ordered, a piece of gutta percha tissue considerably larger than the lint must be applied over the lint, no portion of which should be left uncovered; but if an evaporating lotion be required, the tissue must be omitted, and the application frequently changed and never allowed to dry. In washing or syringing a wound a receiver must always be placed to collect the water or lotion that has touched the sore; and if wool be used to cleanse, each piece as used must be placed on a receiver, and never dipped again into the lotion. To place the foot of an ulcerated leg, for example, in a basin of disinfectant, and use one piece of wool to cleanse the wound and surrounding skin is not surgical nursing.

In dressing burns the fresh application should be ready to put on as the soiled one is removed; thus unnecessary exposure to the air, which causes great smarting, is avoided. In every dressing the nurse must

observe strict cleanliness in every detail. Soiled dressings should always be removed by forceps, placed in a receiver at once, disposed of in the manner of the hospital, or burned without delay.

The forceps must be cleansed with a nail brush in soap and water, and either boiled, or soaked in disinfectant for a few minutes before being used again.

Windows should always be closed when a dressing is being done, and every wound should be covered as quickly as possible.

In offensive cases inhalation of the odour must be avoided, and the patient should never be made to feel the unpleasantness of which he is, as a rule, only too fully aware. The nurse must report the effect of the applications.

Cancer patients vary greatly, and by observing that which suits each special case much pain may be avoided. In dressing extensive cancerous surfaces a styptic should be at hand in case of hæmorrhage; in these cases, and for gangrene, burns, etc., gentle, firm handling is needed, combined with quickness and lightness in removing and reapplying dressings.

In padding splints evenness is ensured by lacing the padding down the back of the splint with strong thread, so that it can be regularly tightened. Special care must be given to ensure the edges being well protected, or pressure sores may arise. Children's splints, and others likely to be soiled, can be covered in addition with jaconet, which can be cleansed easily. In **preparing for extensions** the nurse must have ready a long even strip of strapping, known as the stirrup (preferably on holland), cut with regard to the width and length of the limb; also two or three thin strips long enough to go at least twice round the limb diagonally, to avoid any arrest of circulation: the block, pulley, cord, the weight ordered, sand-bags, and a couple of thin flannel bandages must also be at hand. If the nurse be desired to apply an extension in cases of hip disease, the ends of the stirrup must be well above the knee (quite halfway up the thigh), and the loop so arranged that its sides are exactly equal in length, the block and cord with the attached weight being in the centre. The block is easily fastened to the stirrup by a length of strapping extending from above the ankle on each side, and is applied with its adhesive side to the stirrup, so that the block is enclosed between the strips. It may be further secured by a strip wrapped round on each side of the hole through which the cord passes. The strips which keep the stirrup in position must not be too tight, and the edge of the lowest one must be kept from chafing the skin just above the heel. The patient must be kept flat, with only one pillow, the foot of the bed raised, and the limb retained in position by sand-bags; careful washing and powdering are necessary, when the extension is changed, to prevent chafing of the skin, turpentine being used to remove the adhesive material from the skin.

The art of even **bandaging,** applied intelligently after due anatomical instruction, is very important. The bandage should be gently yet firmly applied, alternate slackening and tightening avoided, also any jerking or pulling. In dealing with an injured limb it should be lightly, yet

firmly grasped, supported as much as possible, and moved evenly. To carry it on the palms of the hands gives less pain than holding it in the fingers.

In receiving accident cases in a ward orders will be given as to bathing, etc. If the accident be a fracture, fracture boards must be placed under the mattress in the bed, and the splints suitable for the case, according to the use of the hospital, should be got ready, padded, etc., and, if necessary (*i.e.* in fractures of thigh), an extension prepared. In removing the clothes the patient must be kept recumbent for fear of syncope in consequence of shock, and the garments removed as gently as possible. Trousers, coat-sleeves, shirts, socks, etc., can all be divided at the seams, and lifted from the injured parts, which should always be freed first. The same applies to a woman's garments; skirts can be slipped downwards by raising the back slightly, and pushing down the bed underneath to make room for them to be drawn away.

The necessary washing must be done between blankets, one being placed on the bed before the patient is laid in it, and another over him; the nurse must watch for signs of exhaustion. Turpentine is useful to remove stains from the hard skin of hands, feet and knees, but it must be well washed off with soap and water to avoid irritation. Except in the neighbourhood of scalp wounds hair must never be cut without a direct order from the doctor. In head injuries the nurse must report any discharge from ears or nose, any peculiarity of the eyes, and if there are fits, she must specially observe where the convulsive movements commence. In abdominal cases, swelling, tenderness in any special area, bruises, etc., must be reported; also all cuts, scars, wounds, ulcers, skin eruptions, vomiting, discharges or hæmorrhage; in fact, anything at all abnormal. After washing, the blankets are removed, and if the patient be cold or collapsed, hot bottles securely wrapped in flannel may be applied to the extremities. Fractured limbs must be steadied by sand-bags, and if the bed-clothes press on any injured part a cradle must be used to support them. No stimulant must be given without direct orders.

In preparing a patient for **operation** the nurse acts under the orders of the surgeon; it is usual to give an aperient over-night, a simple enema early in the morning, and no solid food or milk for at least four hours beforehand, a cup of good beef tea being given about two hours before the appointed time. Antiseptic compresses are often ordered to the place where the incision will be made. If a woman, the hair must be arranged in two plaits for future convenience, and the catheter may be ordered shortly before the operation. Ordinary bed-clothes are usually worn, with a special wrapper. The arrangements at the operation depend on the custom of the hospital; but the nurse is often required to wash sponges, hand instruments, and even to support a limb. Sponges or wool pads must be squeezed as dry as possible before handing to the surgeon, and the exact number counted. The table is prepared by folding a blanket double on it, and covering this with a large mackintosh, over which is a sheet. A low pillow and a draw-sheet are usual, with

small mackintoshes and towels tightly wrung out of a disinfectant lotion, and arranged to suit the special case. A hot water bed is sometimes used, placed next the table. The bed to which the patient is afterwards taken must be well warmed by hot bottles, and a warm water-pillow may be ordered. A receiver and a couple of soft towels must be in readiness in case of vomiting after the anæsthetic.

After-Care. — In moving a patient back to bed the head should be kept as low as possible, and careful attention given that before complete consciousness is recovered the dressings are not disturbed, nor the patient allowed to raise himself hurriedly, for fear of hæmorrhage or syncope. In amputation cases a tourniquet should be within reach of the nurse, to be applied if hæmorrhage occurs, until the surgeon can be summoned. Every detail regarding nourishment, stimulants, opiates, use of the catheter, etc., must be obtained from the surgeon.

After an operation the dressings should be inspected at frequent intervals, and if discharge or blood soak through them the fact should be reported at once. If the surgeon be not at hand the dressing should be "packed," *i.e.* pads of absorbent wool bandaged over the points where the discharge appears.

No food should be given for some hours after an operation, unless specially ordered, or the effects of the anæsthetic have passed off; but small pieces of ice, a little soda water, or a teaspoonful of hot water may be given to allay thirst and relieve vomiting. If the latter be severe, it should be reported.

The nurse should have all in readiness for **the visit of the surgeons to a ward.** Hot water, towels, disinfectant lotion for hands and instruments, dressing forceps, probe and director, and a tongue spatula immersed in lotion should be carried round by the nurse; and artery forceps, bistoury, etc., should be in readiness if required: a good lamp should always be ready, and a receiver for soiled dressing, prepared notes of cases beside each patient, splints, etc., so that no unnecessary delay is caused.

Medical Nursing. — The ventilation of medical wards is most important, the temperature must be higher — usually fron 60° to 65° F. — and yet the air kept quite fresh. It is advisable to have two or more thermometers in each large ward, to ensure an evenly-distributed heat. In small wards, where a moist and higher temperature may be required (70° F.), draught may be avoided by the Hinckes Bird method of ventilation, *i.e.* a piece of wood, three or four inches deep, exactly fitting the window frame, is placed so that the lower sash closes on it, and the outside air passes up between the upper and lower sashes in the middle of the window, and is directed upwards into the room.

To give an accurate report, the use of **the clinical thermometer** needs greater care than is often bestowed upon it. If given to a patient able to hold it in the mouth, it must go under the tongue, and be held by the closed lips (not by the teeth), for always the same time, at least five minutes. The so-called "half-minute" thermometers are deceptive if used for this interval. If placed in the axilla the skin must first be

dried, and the thermometer so inserted that the bulb touches the skin on every side, the arm being drawn across the chest; if necessary, the arm must be held there for the required time. In children the fold of the groin is often convenient, or the rectum. In every case the record should be written down at once, not trusted to memory, and the thermometer placed in "$\frac{1}{20}$ carbolic," or "$\frac{1}{500}$ perchlor.," for a few minutes before replacing it in its case. It is a good plan to dip it into clean water, and wipe it with a clean napkin, before giving it to each patient, especially if used in the mouth. The temperature of a patient in a bath or pack must never be taken in groin or axilla.

Accurately counting the rate of the **pulse,** and reporting its character, are matters of training and experience, and of great importance. A nurse should be able to notice the more important changes that may occur, also whether drugs, stimulants, etc., produce any marked effects.

It is better not to let the patient know when the *respirations* are being counted, as this may alter the rate, and this record is at times of more value to the doctor than that of the temperature.

Bed-making is one of the most important duties of a nurse. In hospital wards where the beds, mattresses, etc., are of right size and height, no special difficulties arise. A single blanket is spread over the hair mattress, and over this a sheet, the upper end of which is rolled round the bolster, not spread over it, and tucked firmly in all round. A draw-sheet, consisting of a sheet folded about three feet wide, is placed across the bed, one end being tucked in at one side, and the extra length flatly folded and tucked in on the other. If necessary, a square of mackintosh is placed under the draw-sheet, and may conveniently be kept in place by a small safety pin at each corner. The top sheet and each blanket should be put on and tucked in separately, and the feelings of the individual patient consulted as to folding back blankets or quilt at the top. The quilt should be so pinned or folded that it does not touch the floor at the bottom or sides of the bed, and prevent free circulation of air underneath.

In *changing bed-linen* for a helpless case the upper sheet and quilt must first be removed, and the patient covered with his blanket or blankets; he must then be gently turned on one side (if possible the right to avoid any risk of syncope in cardiac or pleuritic affections). This can be done with little effort by means of the draw-sheet; this is then, with the mackintosh, rolled up tightly towards the patient, the bottom sheet untucked, also rolled up tightly, and with the other pushed well under the shoulder and buttocks of the patient. The clean sheet, draw-sheet, and mackintosh are also rolled up together lengthwise for half their width, and placed close to the patient, the other portion being smoothly spread over half the bed. For a weak patient this is a good opportunity for washing the back and applying spirits and dusting powder, so that he need not be disturbed again. The patient is then turned back over the rolled linen, and just turned sufficiently to the left side to allow the soiled linen to be removed; the clean roll is then drawn through and evenly spread over the other half of the bed, and all well tucked in. It facilitates

matters to raise the feet and legs, and place them on the clean linen before turning the patient back, and the head should always be comfortably supported by pillows. The top sheet can be passed in under the blankets from the bottom of the bed, and then they are separately tucked in and the quilt replaced. By placing the rolled part of the sheets, etc., *next the bed*, the hands can be slipped underneath it, palms upwards, to draw it through; thus the nurse's knuckles are not pushed against the back of the patient. Heavy bed-clothes must always be avoided, and the feelings of the patient consulted as to warmth whenever possible.

In *removing body linen* of helpless patients, it is well to draw it up from the back, and, having unfastened the collar, to bring the garment over the head, taking the arms out of the sleeves last. In putting on fresh linen, it is easier if the arms be first placed in the sleeves, and then the shirt lifted over the head, and drawn down at the back. Where all movement is undesirable, a shirt or night-dress can be divided down all the seams of one side, neck, shoulder, sleeve, etc., and fastened by tapes; it has then only to be put on at one side, and the back rolled and passed under the patient like a draw-sheet.

Medical Examination. — The nurse must be ready to remove and adjust all personal or bed clothing for medical examination. When the abdomen is to be examined the quilt and blankets must be turned back but the sheet left upon the patient for the medical attendant to arrange for his own convenience.

Helpless Cases. — In changing the bed-linen for cases which must not be turned at all on either side, the dirty under-sheet, with mackintosh and draw-sheet, can be rolled up from the bottom of the bed, and pushed well under the buttocks; the rolled part of the clean linen is now laid close to it, and the lower part of it spread and tucked in at the foot of the bed. By gently raising the buttocks the two rolls are passed underneath, and the patient now rests on the clean sheet. The upper part of the soiled sheet is then rolled and pushed well up under the shoulder-blades, and the clean one also; and then, by gently raising the shoulders a very little, both are drawn up to the top of the bed, the dirty linen removed, and the clean spread smoothly. By changing from below upwards, the patient is not pulled down the bed, which entails the extra fatigue of lifting up again.

Lifting is readily done by two persons, who pass hands — left or right as the case may be — under the buttocks, and the other hands just below the shoulder-blades, while a third helper, if the patient be very weak, supports the head and shoulders. By lifting *exactly simultaneously*, the heaviest patient can be raised without over-exertion. Or two assistants may grasp the draw-sheet close to the buttocks and under the shoulders, the head being supported as before, and the patient raised, but this is apt to bring the draw-sheet too far up the bed, and the patient is pulled down again in endeavouring to rearrange it. A pillow is useful in abdominal cases where the knees are drawn up; and it can be efficiently protected by placing a piece of mackintosh round it under the pillow-case. When

used to support a limb it is more comfortable if hollowed in the middle so as to form a trench.

When a **cradle** is used to keep off the weight of the clothes, a thin blanket or the sheet should be upon the patient.

Water-beds and water-pillows are filled with lukewarm water, so as neither to chill nor overheat the patient. They should be covered by a mackintosh and thin blanket under the sheet. A water-bed must be filled before the patient is placed in it, but a water-pillow can, if necessary, be slipped in empty underneath him as he lies.

The nurse should be careful that the patient is in the middle of a water-pillow, as if allowed to rest on the edge bed-sores will form.

Bed-rests are useful when the patient needs to be more or less upright — special care is needed in such cases to prevent the formation of bed-sores, as extra pressure is thrown upon the sacrum and buttocks, and in these cases the circulation is usually defective.

When a patient has been ordered to be placed between blankets, as in acute rheumatism, those next him should be frequently changed, and a draw-sheet should be always used to keep the back in a good state. Flannel night-shirts must be worn.

Bed-sores. — The prevention of bed-sores consists in cleanliness, dryness of the skin, and smoothness of the bed-linen. Except, perhaps, in some very rare cases of cerebral and spinal disease, when they are said to form with appalling rapidity, bed-sores are *always* preventable; indeed, it is with some hesitation that I allude to any possible exceptions. In such cases as fevers or general paralysis bed-sores need never be seen.

Constant cleanliness and watchfulness, a vigilant eye to discharges, attention to the smoothness and dryness of the sheets, and judicious changes of position, are the secrets of success. If waterproof sheeting must be used a considerable thickness of linen and blanket should lie between it and the patient's skin. The use of water-pillows or beds is imperative in long or severe cases, and, being made of smoother material, are preferable to air-beds or pillows; they are also more elastic. All parts exposed to pressure and soiling must, at least twice daily, be washed with soap and water, well dried, rubbed with spirit, and dusted with powder. A useful mixture is one part boracic powder to two of starch powder. If inclined to be tender, the skin may be painted with collodion or balsam of Peru and powdered. When it is difficult to maintain dryness, lanoline or zinc ointment may be rubbed in and powdered.

Dryness of Bed. — When there is no control over bladder and rectum, careful and frequent cleansing and changing is necessary. Incontinence of urine may be met by the use of glass urinals for either male or female cases, supported by pads of wood wool or carbolised tow in butter muslin; in the former cases care must be taken to avoid pressure on the scrotum; and, in both, absolute cleanliness and frequent dusting with powder is essential to avoid chafing. In female cases the vulva, particularly within the labia, must be attended to carefully. When there is loss of control over the rectal sphincters, similar pads on a piece of

mackintosh may be advantageously used; they can easily be removed, destroyed, and new ones applied. In washing stout patients, especially women, the parts under the breasts and the folds of the groin and thighs need careful drying and powdering, as neglect may soon cause eczema or painful sores. Nurses cannot have too constantly before them the suddenness with which sores may appear after what may seem to them but a trifling neglect.

When bed-sores have formed the treatment is in medical hands. The nurse may be desired to apply charcoal poultices to separate sloughs, and to irrigate the wound with creoline $\frac{1}{40}$ carbolic or sanitas, cutting away the slough as it becomes loose. She may have to protect bony excrescences by pads made of several layers of lint, with a hole in the centre over the wound, secured by strapping, and not removed, if possible, for two or three days. Iodoform and dressings of resin, zinc, or other ointments may be ordered, and in such cases the dressings must be laid on the wound only.

The physician or surgeon requires faithful reports of all that occurs to the patient between his visits — hence the importance of a nurse trained to accurate observations and statements, familiar with symptoms, and aware of their practical indications.

For example, in enteric fever the physician should be informed on the following points: —

1. Temperature, every four hours, in mouth or axilla, as desired.
2. Pulse, at same intervals, with statement as to strength and variation, if any, at any stated times; or after food, drugs, stimulants, etc.
3. Respirations, at same intervals; cough is important as a warning of lung complications.
4. Stools. Frequency, colour, and character, noting if undigested food be passed, blood, etc. If much flatulence.
5. Amount of urine and its colour — watch for symptoms of retention.
6. Vomiting. Frequency and nature, whether rejected food, such as curdled milk, or "coffee grounds," etc.
7. Any eruption, characteristic or otherwise, to be watched for and reported; also abdominal pain, tenderness or distension.
8. Amount of sleep, exactly: its character — restless or quiet; whether delirium, muttering, twitching of muscles; also, manner of waking — quietly or with a start.
9. Condition of skin, dry or moist — of tongue, and amount of sordes on teeth. The mouth and teeth should be frequently cleansed by lint or linen wrapped round the forceps dipped in the lotion, and gently passed round the mouth; and, if able, the patient should be encouraged to rinse the mouth and gargle with the prescribed wash.
10. The exact kind and amount in ounces of the nourishment taken, the hours when it was given, and the readiness or otherwise of the patient for it; also, the amount of stimulant and medicine, and the times of each.

11. Effect of any drug prescribed for temperature and pulse; or, if for sleep, when sleep is induced, how long after, and for what length of time.
12. Effect of sponging, if ordered; when done, for how long, and the result as shown by temperature, pulse, respiration, sleep, and general condition.

Such a report should be written both by the day and by the night nurses for each other, to ensure that no important change is overlooked.

In *Pneumonia* the rules for temperature, pulse, and respiration would be the same, with a report on cough, expectoration (its colour, consistency, whether difficult, profuse or the reverse); pain in any particular place; effect of hot or cold applications; amount of sleep; amount of nourishment; evacuations, etc.

In *acute Rheumatism*, temperature, respiration, and pulse; pain, its locality and intensity, specially if in cardiac region; breathlessness on the least exertion; state of joints; evacuations; condition of urine; action of skin, etc. Effect of medicine, and any special symptoms connected with it, such as deafness and noises in the head after salicylate of soda, quinine, etc. Effect of sponging or other treatment, amount of sleep, exact amount of nourishment, etc. Nothing is too small to report, especially with regard to the action of medicines and drugs.

Effect of certain Drugs. — The nurse should be able to recognise the more important effects of these, such as —

In connection with opium — drowsiness, contraction of the pupils, heavy breathing, constipation.

While digitalis is being taken the pulse must be carefully noted.

Diarrhœa or sickness may result from the use of arsenic.

Quinine may produce headache or noises in the head.

Salicin or the salicylates — deafness, excessive perspiration, and headache.

Mercurial treatment may produce tenderness of the gums, salivation and diarrhœa.

Iron preparations turn the tongue black, and produce very dark, almost black stools. Bismuth has a like effect.

When antipyrin and like febrifuges are given, the nurse must watch for any symptoms of collapse, as occasionally patients do not bear such drugs well.

In administering medicine the nurse should ascertain whether it is to be given before or after food. Quinine is usually taken before a meal, iron and arsenic afterwards. Cod liver oil is digested more readily after food.

Administering of Medicines. — All medicines must be accurately measured in a graduated glass, as spoons vary greatly in size. "Drops" also must be measured in a minim glass. The glasses must be washed directly after use, and, if in a ward, between each patient. Medicine bottles should *never* be put down near lotion or liniment bottles.

The special applications required in nursing are many, and a trained nurse should know the best possible way of dealing with them.

Poultices need dexterity to make them of the right size and weight for the case. If jacket poultices be ordered, the nurse must prepare two pieces of calico, shaped at the neck and under the arms, so that the poultice covers the sides of the chest from the axilla downwards. Two pieces of thin mackintosh, a little larger and similarly shaped, sufficient cotton wool to cover both chest and back, a poultice jacket, safety pins, linseed meal, a spatula (ordinary painter's), a basin, and boiling water are also needed, and, if the poultice be made at any distance from the patient, two hot plates. The basin and spatula must be made hot, sufficient boiling water poured in to make the required poultice (about ¾ pint for an adult), and the linseed sprinkled in, being well stirred all the time. A well-made poultice when turned out should leave the basin quite clean. It is then quickly and evenly spread by the spatula, the edges (not more than half an inch wide), neatly turned over, rolled up, placed between the hot plates if necessary, and brought to the patient. He must previously have been placed on one side, with the night-shirt ready to be pulled well up at the back, if he be too weak to have it removed. The poultice is then half unrolled and applied, care being taken not to injure the skin, though this is not likely if the poultice be not too wet. It is next covered with the jaconet and a layer of cotton wool, both half rolled, also with the poultice jacket; the shirt is then pulled down, the patient turned on his back, and the rolled part of poultice, wool, etc., brought round to the other side. The front half of the poultice is made in the same way, applied to the chest, covered with jaconet, wool, and the jacket; then both are secured by safety pins on each shoulder, and down the sides, the poultice jacket being pinned down the front. The shirt is drawn down, and the patient should have some nourishment after the fatigue. Well-made poultices thus applied retain their heat for many hours. Sometimes the poultice is placed in a bag of flannel, but these require more frequent changing, and more care lest the skin be injured by applying it too hot. A little oil spread over the linseed is soothing if the skin is becoming tender.

"*Poultice*" or "*Pneumonia jackets*" are garments made of a strip of thin flannel or flannelette, the right width for the patient, shaped at the neck, and well cut out under the arms, meeting in front and overlapping a little. They are lined with a layer of cotton wool neatly tacked in, and can easily be placed over the poultice, and secured on the shoulders and down the front by safety pins, which are firmer and more comfortable than tapes. In bronchitis cases also this is useful, and the poultices can be changed without removing the jacket. In pleurisy a band of flannel pinned firmly round the lower ribs gives relief by restraining muscular movements.

Charcoal poultices are made of equal parts of charcoal and linseed mixed in the same way — usually ordered for sloughing wounds.

Mustard poultices are conveniently made by adding the proportion of mustard ordered to the boiling water, and then stirring in the linseed.

Mustard plasters are made by spreading thickly-mixed mustard on a square of brown paper of the exact size ordered, and covering it with a piece of muslin. Mustard and any proportion of flour may also be mixed and applied in the same way. Mustard leaves are dipped in tepid water and placed on the spot. These applications are left from ten to twenty minutes, as ordered; and, after removal, the skin must be covered with a layer of cotton wool.

Bread poultices are conveniently made by placing the crumb of white bread (stale if possible) on a piece of calico or small towel across a basin, pouring boiling water over it, wringing as dry as possible, placing between muslin, and applying, with jaconet and wool over, as before.

Blisters. — In applying blistering fluid, none must touch the skin except at the place ordered, and the cover of cotton wool must not be strapped at all tightly, or pain will ensue as the blister rises. If a plaster be used, and the blister do not rise, after an hour a small poultice may be applied, which usually produces the desired effect. In cutting the raised cuticle, the small snip should be at the lowest side of the blister, and wool arranged to catch the fluid. If it is to be kept open, all the raised skin must be cut off, and the dressing applied exactly to the sore: if not, a simple ointment dressing is usually put over the skin, and secured by wool and strips of strapping.

Liniments must be applied always to both chest walls if ordered for bronchitis, etc., and in every case rubbed in with the palm and not with the fingers. Painting with iodine must not be continued without orders when smarting follows the application.

Fomentations and stupes are conveniently made of a length of flannel doubled. This is placed on a strong towel over a basin, boiling water poured over it, and the towel then wrung out quite tightly; a good wringer is made by a strip of ticking sewn at both ends, and a stick passed through each. They are applied to the painful place, covered with thin mackintosh or jaconet, — at least one inch wider in every direction than the fomentation, — and a layer of cotton wool; and are kept in position by a flannel binder or bandage. Such stupes may be made with decoction of boiling poppy-heads, or may be sprinkled quickly with 40 to 50 ♏ turpentine or 10 to 30 ♏ tinct. opii, as may be ordered, just before application.

In **applying leeches,** the skin must be well washed with hot water, and plain (not scented) soap; the leech is placed in a test tube, medicine glass, or small tumbler, half full of cotton wool, held over the place. If slow in biting, a little milk may be placed on the patient's skin, which usually succeeds if the leeches are good ones. They fall off when full, but if they remain too long, a little salt sprinkled on them will remove them at once. They should be handled as little as possible before being applied.

Orders will be given about the amount of bleeding desirable — a warm poultice over the bites encourages it. If to be arrested, a very small piece of cotton wool, a mere film, placed in the bite generally

causes coagulation. Failing this, pressure, cold applications, or a styptic, such as balsam of Peru, may be tried, and the medical attendant must be informed. Leech bites must be noticed from time to time for some hours lest the bleeding begin again. The patient should not be alarmed or agitated, either in the application of the leeches or in controlling the bleeding. If leeches are pulled off they are apt to leave their teeth, which form a tiresome little wound.

Dry cupping is done by exhaust glasses, or by placing in a cupping glass or small tumbler a small piece of blotting paper dipped in methylated spirit, setting it alight, and at once applying. The edges of the glass should be previously oiled, and it is easily removed by pressing away the skin from the edge, and allowing air to enter.

In administering **enemata,** the nurse should be able to give them equally well whether the patient is lying on the back or side. Generally, however, he is placed on the left side, with the buttocks close to the edge of the bed, and the knees flexed. The nurse, having the enema ready, lubricates the nozzle of the syringe with a little oil or vaseline, and seeing that it is full, so as not to inject air, with the forefinger of her left hand, also lubricated, ascertains the entrance to the rectum, and gently inserts the nozzle with her right hand. Great care must be taken if hæmorrhoids, fistula, or fissure be present, all exquisitely tender. In cases of fæcal accumulation, the nurse may be desired to break up the mass gently with her finger well oiled, and her nail filled with carbolic soap; she must also give the enema at intervals. When this is so, or when there is irritability of the bowel, or relaxation of the sphincters, the gum elastic tube supplied with the Higginson syringe is useful. It is softened by immersion in hot water, well oiled, fixed to the syringe or irrigator, and gently inserted. I find this tube safer and better to use as a general rule. Indeed the short, hard bone nozzles usually supplied for rectal use, are not to be recommended: it is better always to draw three or four inches of stout rubber tubing over them before insertion. The bed should be specially protected by a mackintosh and folded sheet. Restoratives should be within reach as some patients turn faint after the operation. In this, as in douching, washing backs, etc., no exposure of the patient is necessary or justifiable.

Simple enemata should not be made with scented or medicated soaps, curd or yellow is the best.

Starch enemata are made by mixing from a teaspoonful to a tablespoonful of starch powder, according to the quantity required, with a little cold water into a smooth paste, and then adding boiling water until a mucilage is formed, to which the special medication is added. For a starch and turpentine enema, ℥ j. turpentine to ℥ xv. starch mucilage may be ordered; for a starch and opium, the prescribed number of minims of opium are added to the prescribed number of ounces of starch mucilage.

Castor and olive oil enemata are conveniently given by warming the oil in a cup, and then placing the cup in the basin containing the simple

enema which usually accompanies the oil. The end of the syringe is readily transferred from the water to the cup after ℥ij. or ℥iij. have been injected; and when the oil has been given, it is readily replaced in the water without fear of admitting air.

In *rectal feeding* it is desirable, when possible, first to wash out the lower bowel by a small enema of warm water. The quantity and materials of a nutrient enemata vary according to special orders; they are most easily given by a ball syringe holding the right number of ounces. The tube, being longer and thinner than that of the ordinary syringe, is less likely to irritate the bowel, and cause the enema to be returned. It must be carefully cleansed after use each time. Nutrient enemata must be given very slowly to ensure retention, not a bubble of air should find its way into the bowel, and a napkin should be held to the anus for a few minutes after: in all these applications great gentleness is essential.

Glycerine enemata are usually given in a special syringe holding the exact amount required.

In **nasal feeding** the nurse must be careful that the tube is really in the œsophagus, and only administer ℥j. to ℥ij. at a time. Nasal feeding, however, should always be done by a carefully instructed person, if not by a surgeon [*vide* art. on "Dietetics," p. 387].

In passing the **female catheter** the vulva must first be thoroughly cleansed with warm water, and a disinfectant, $\frac{1}{4000}$ perchloride, $\frac{1}{60}$ carbolic, creolin, or Condy. The patient should lie on her back with the knees drawn up, though in some cases (*e.g.* ruptured perinæum), she is better on her left side. The catheter — generally a gum-elastic or flexible india-rubber one, size seven or eight — must be perfectly clean, not rough at all on the surface, and soaked before using in $\frac{1}{4000}$ perchl. or $\frac{1}{40}$ carbolic. It is lubricated with carbolised glycerine or vaseline, and the nurse, holding it in one hand, with the index finger of the other also lubricated, finds the entrance to the vagina; just above this the hard round meatus urinarius (with its depressed central orifice) is easily felt, and the catheter passed into it, the other end being placed in a convenient receptacle. If there be much vaginal discharge, or the nurse cannot pass the catheter into the orifice at once, the catheter must be thoroughly recleansed, and the nurse, separating the labia, must ascertain the position of the meatus by the eye, and insert the catheter after carefully wiping all discharge away; it is most important that no discharge be carried into the bladder, as there is great danger of cystitis if the strictest cleanliness is not observed. Glass catheters can be boiled each time after use, and no impurity can remain unnoticed, but there is danger in their fragility. A catheter must be thoroughly cleansed in warm water, held under a tap to allow the water to run from the eye downwards for a few minutes, and then placed in a disinfectant. If boracic lotion be used, care must be taken that crystals do not become deposited on the catheter, as one used in this condition may injure the urethra. Any

marked tenderness in passing the catheter must be reported, as it may be due to urethral caruncle or other special cause.

In *washing out the female bladder* the catheter is passed in the usual way, and the water drawn off. The nurse has ready in a jug the prescribed quantity of the warm lotion to be used (frequently "boracic"), and an india-rubber tube, about one yard long, to which is attached a glass funnel holding ʒiv. to ʒvj. The free end of the catheter is placed in the tube, which the nurse compresses a few inches above the catheter between the second and third fingers of her left hand, holding the funnel between her thumb and index finger. With the right hand she fills the funnel and tube from the jug, and then, releasing the tube and raising the funnel, she allows the lotion to flow into the bladder, compressing the tube again just before the funnel empties itself. After repeating this once, or even twice, she removes the tubing from the catheter, and allows the bladder to empty itself. It is wise to have a glass measure to receive the contents of the bladder, in order to ascertain either that no lotion remains or only the right number of ounces ordered. The tube is then readjusted, and the process repeated until the prescribed quantity of lotion has been used. The nurse must carefully examine the catheter lest the eye become blocked by mucus, as is often the case in cystitis.

In giving **vaginal douches** the nurse should protect the bed with a piece of mackintosh and folded sheet. The patient should lie on her back, with head rather low, and a pillow under the loins. The bed-pan should be warmed before being used, and a towel be at hand.

Having prepared the douche as ordered, *testing its heat by the bath thermometer*, and, if of Condy's fluid, not making it too strong (ʒj. to Oj. of the fluid, or two or three crystals of the permanganate), the nurse lubricates the glass nozzle with carbolised glycerine or vaseline, and allows it to fill with the lotion, to exclude air. Having placed the irrigator at a convenient height above the bed, she inserts the tube gently into the vagina, unless the patient prefer to do it herself, which may be better in cases of cancer, etc., where there is great tenderness. The tap is then turned, the douche given, and the tube removed without allowing any air to enter. If a Higginson's syringe be used, the glass nozzle is easily fixed to it by removing the bone nozzle, and putting the glass into the india-rubber tube; it is then filled with lotion, and inserted in the same way. The douche is conveniently contained in a jug supported at the side of the bed. Glass nozzles (without a terminal hole, lest the nurse unwittingly administer an intra-uterine douche) are the cleanest and safest, as they can be boiled and left to soak in disinfectant until wanted. If hot douches are ordered (110° F.), the vulva may be smeared with a little carbolised vaseline to protect the skin, which is often very sensitive. The bath thermometer should invariably be used, and a careful report given of the result of the douche.

Vaginal plugs and tampons are made of absorbent cotton wool, rolled into the required shape, and secured by linen thread. Tampons

are pear-shaped with the thread attached to the lower end, and are generally used for applying medications to the vaginal walls. Plugs may be made by turning in the edges of a square of wool, and forming it into a sausage-shaped roll secured in the middle by a long thread. For supporting the uterus and packing round the cervix several of these rolls are attached to the one string, forming the "kite tail" plug. For plugging with a speculum, rounds of cotton wool, of varying sizes, with the thread passed through the middle, are convenient. In every case the threads should be long enough to be well beyond the vagina, and the exact number of plugs inserted noted down.

Gynæcological Work. — A nurse should understand how to arrange a patient for examination, bringing her well to the edge of the bed on her left side, the spine as nearly as possible in a line with it, the knees flexed, the right one being rather more drawn up than the left, and the left arm brought round to the back, so that the patient is lying almost on her chest.

She should also know the names of the various specula (Ferguson, Sims, etc.), and be able to pass them if required. This is done by placing the two first fingers of the left hand, previously lubricated with carbolised vaseline or glycerine, in the entrance to the vagina, and drawing the perinæum backwards so as to admit the edge of the speculum, which is passed gently in a backward direction, holding the perinæum well back so as to avoid touching the clitoris, or causing pain, until the os can be seen. It may be necessary to alter the position of the speculum a little, if a "Ferguson," to bring the os into view, in order to carry out special directions for plugging round the cervix in any given way. The nurse must be able to prepare uterine probes for use, by placing a very thin layer of cotton wool on her left palm, laying the probe at the edge of it, and, by a little manipulation and rotation of the instrument, wrapping it smoothly and firmly round. After use the wool is removed and fresh supplied. Medicated bougies are placed in the vagina to dissolve. Suppositories are gently passed into the rectum, the finger being previously oiled.

Hypodermic injections are given, after seeing the needle is clean and firmly screwed on, by first accurately filling the syringe, and then driving the fluid to the point of the needle so as to expel the air. The skin, previously cleansed, is then firmly held and raised into a fold, while the needle is gently but quickly inserted into the fold in a direction nearly parallel with the surface, and pressed onward till the point has passed through the skin into the subcutaneous tissue; the syringe is then emptied and withdrawn, a finger being placed over the puncture for a minute or two. If the needle is properly inserted below the skin no bleeding or swelling will ensue. The same care must be taken in purification of this syringe and its parts as of other instruments.

Baths. — In giving baths everything must be ready before the patient is disturbed, and the temperature verified by the thermometer. In a large bath the hot and cold water must be well mixed before this is

done, and on no pretext whatever should any patient be left with the taps running. The cold water must always be turned on first, and no patient or junior assistant should ever be permitted to touch the taps. Except under special circumstances — such as the special treatment of fever, and then only by the charge nurse — the taps should never be turned after the bathing has commenced.

Towels, a blanket, and if necessary a screen should be in readiness. The temperature is ordered to be from 98° to 110° F. for hot baths, 92° to 98° warm, 85° to 92° tepid, and 70° cold, and the water must be tested by the thermometer during the length of time ordered. That the bath may not fall below the degrees required, the water should stand a little above these limits at first, and should have lain long enough in the bath to warm it through. Thick stoneware baths absorb a larger quantity of heat. The patient has a blanket laid over him, and as he is lowered into the bath, this remains spread across it, and is wrapped round him again when lifted out.

With children the blanket may be spread over the bath first, and they are then rolled in it and placed in the bath.

In giving a hip-bath the same arrangement is desirable, and a small blanket can be placed over the shoulders to avoid chill.

Warm towels and wrapping in a blanket are desirable after hot baths, the bed being warmed by a hot bottle.

In cold bathing we are usually ordered to lower the patient in a sheet into tepid water (75° F.) first, and to reduce the temperature by adding cold water gradually.

Of special baths the following are usually ordered: —

(*a*) Mustard, ℥ij. to ℥iv. to every 4 gallons water.

(*b*) Salt, 1 lb. to every 4 gallons water.

(*c*) Alkaline, carbonate soda or potash, ℥ij. to ℥iv. to every 4 gallons water.

(*d*) Sulphur, sulphide of calcium, ℥ij. to ℥vj. to every 4 gallons water.

The time for which the patient remains in the bath is ordered by the medical attendant.

Vapour and hot air baths can be administered in bed, by covering the mattress with a waterproof sheet and a blanket. The patient is stripped and placed in a blanket, with another over him. A long cradle is then placed in the bed, well covered with blankets, so as to exclude all air except at the foot, where a funnel over a special lamp, or from a steam-kettle on a lamp, conveys the heated air into the bed. Hot drinks, such as milk, hot water, etc., may be given with advantage to promote perspiration. The temperature should be taken before, during, and after; and the pulse felt at intervals, in case of faintness. After the stated time, usually from twenty to thirty minutes, the hot air or steam is withdrawn, the patient wrapped in hot dry blankets, and left a while before dressing him and remaking his bed.

If the bath be given out of bed, a lamp, specially protected, is placed

under a cane-chair, which is covered all round by a blanket; the patient is undressed, wrapped in blankets, and placed on it with a screen round. The same routine is followed after the time has elapsed, except that the bed should be warmed by hot bottles.

Hot and cold packs are given by placing a patient on a bed similarly prepared as for the air-bath, and enveloping him from head to foot in a thin blanket wrung out of hot water for the hot pack, or a sheet wrung out of cold for the cold pack. If the latter be to reduce the temperature it may need renewing after an interval, the temperature being taken in rectum or mouth before and at frequent intervals during the process. A cold towel should be on the head. The patient in both cases is to be left for a time before being dressed.

Icebags should be filled with small pieces of ice, and have a piece of lint or linen between them and the skin. If for the head they must not be too heavy, and may be tied to the top of the bed to support them. They must never be left until the ice is all melted.

A tent and steam kettle are often ordered for bronchitis, tracheotomy, etc., and can be made of folding screens covered by quilts or blankets so as to exclude all draught, and enable the space to be filled with steam. The kettle must not be too high above the patient, or in a position to allow it to drop or spurt on him; especially with young children an equable temperature must be maintained, and the supply of steam be constant.

Inhalations are given in an inhaler, or in a jug with a towel placed round it so that the patient breathes only the steam. Water at 140° F. must always be used, and care taken that a weak patient does not become faint by bending over too much in a crouching attitude. The nurse should be familiar with the use of asthma powders, nitrite of amyl capsules, etc.

Sick Cookery. — *Gruel.* — A nurse should understand the making of gruel by mixing the fine oatmeal or grouts into a smooth paste with a little cold milk or water, and then pouring it into the boiling milk or water, and letting it boil some minutes after thickening, stirring meanwhile to keep it smooth. Arrowroot and cornflour are prepared in the same way. White wine whey is made by adding ℥iv. sherry to a pint of milk just as it boils, and then straining through muslin.

Junket is made by adding a few drops of rennet to a pint of lukewarm milk, and letting it stand.

Peptonising milk, gruel, etc., is the nurse's duty, and is conveniently done by means of the various powders or peptonising fluids, according to printed rules. The food must not stand too long, or it will become bitter; the process is checked either by boiling for a few minutes, or placing in ice.

The preparation of raw *beef tea*, scraped raw beef (given with brown sugar in certain cases), raw meat juice, beef tea, mutton broth, veal tea, chicken broth, chicken jelly, custards, etc., are all necessary. The nurse's duty is to give the nourishment in an appetising manner.

Dainty arrangements, small quantities, served regularly and punctually, with as much variety as possible, and absolute cleanliness of every detail, are essential. The nurse must never touch the food with the finger, or taste it with the patient's spoon to test its temperature. In feeding a patient whose head is on the pillow, the nurse's hand, raising the head, must be put under the pillow. The food must be cautiously given, but the food must not be dribbled ineffectually or too slowly into the mouth.

The **disinfection of sputa** from phthisical patients is a necessary precaution. The best spittoons are white mugs with an inverted conical lid. A disinfectant, such as "$\frac{1}{20}$ carbolic" or ʒ ij. creoline in ℥ j. water can be used, and the whole utensil is easily cleansed. Stiff paper may be folded for the same use, but it is not so sightly, and does not allow the sputa to pass readily into the disinfectant. All handkerchiefs used by such patients should be placed in $\frac{1}{20}$ carbolic at once.

Typhoid stools must be freely covered by strong carbolic, or a solution of sulphate of iron, and allowed to stand, if possible, about twenty minutes before being emptied into the drain. The utensil must be closely covered.

It is usual to have a sheet wrung out of $\frac{1}{20}$ carbolic or creoline (℥ iv. to ℥ vj. to 1 gallon of water) over the door of a room in which there is an infectious case. Sheets on folding screens may be placed round a septic case in a ward until it can be removed. The carbolic spray is sometimes ordered also. All bed-linen, and whatever has been worn by an infectious patient, must be immersed in carbolic or other disinfectant at the bedside; they must not be carried across the ward first. Special cups, glasses, etc., must be kept, and, if necessary, boiled or heated in the oven before using again.

Bedding, outer garments, etc., are best purified by the special apparatus which is provided in most hospitals, and in connection with the vestries.

A nurse in attendance on infectious cases must take a carbolic bath, (not forgetting her hair), change every article of clothing, have all garments worn in the room disinfected, and if possible have some days' interval before returning to general work. She must not eat in the room of an infectious case, her hands must be thoroughly cleansed after contact with the patient, and she must rinse the mouth and gargle with Condy's fluid (℥ j. to Oj.) at intervals.

The nursing of children calls for special watchfulness, and that keen and sympathetic power of observation which can distinguish between fretfulness and pain, hunger and temper, caprice and loss of appetite, etc. In nursing fretful children kindness is essential. I need scarcely say that corporal punishment should never be administered.

One very common error is moving sick children about too much. A nurse who would not dream of giving unnecessary exertion to an adult with acute bronchitis or pneumonia, will not realise there is harm in raising a child similarly affected into a sitting position to change linen, poultices, and so forth; and will even take it out of bed to wash it on

her knee by the fire, forgetting that if easy to her to lift and move a child, it by no means follows that it is easy to the child. Sick children should be handled as nearly like adults as possible. Special care is necessary to keep them dry and clean; every two hours by day they should be attended to except when sleeping soundly — when four hours may elapse — and twice at least during the night. Attention after each meal is desirable, and the habit of regularity taught as far as may be. Careful washing and powdering are essential. Flannel or flannelette night-gowns made long, and even to button below the feet, prevent chill when a restless child throws off the bed-clothes in its sleep. When dressing wounds, the attention of the child should be diverted as much as possible, half the crying is from fright rather than pain. Also children should never be deceived with regard to pain, the taste of medicine, and the like; if they find they have been told what is untrue the power of the nurse is gone.

In **clothing infants,** whose ribs are very yielding, there should be nothing tight round the chest or waist; and the legs and thighs should always be covered with flannel or wool, not, as is usual, left naked while the chest is swathed in layers of useless clothing.

In feeding children they must be induced to take the amount ordered; firmness and kindness go far to succeed in this.

When, in whooping-cough, food is rejected from the stomach, it is well to give more as soon as a paroxysm is well over, to ensure that some be assimilated before the next fit of coughing. In convulsions, when a bath is ordered, it ought to be from 90° to 95°, deep enough to immerse the child up to the neck, and the thermometer kept steady by adding more hot water from a can, not from a tap; a blanket is thrown over the bath, and cold or iced applications may be placed on the head.

It is essential to remember that the stomach of an infant a few weeks old only holds a small quantity of fluid, and no more than ℥ j. to ℥ ij. should be given at one time or vomiting will follow.

In feeding infants by hand the bottles must be scrupulously clean; those with the teat on the bottle are the best; the tubes of the ordinary shape are difficult to clean. In either case two must be kept, one being soaked in cold water after a thorough cleansing in hot soda and water while the other is in use.

In cases of diphtheria great care must be taken that none of the discharge or mucus is coughed or spat into the nurse's eyes or face, especially during feeding, and the nurse must not put her face close to that of the child.

In cases of tracheotomy the nurse must keep the temperature of the room perfectly equable, and the steam kettle, usually charged with a disinfectant, always going. A small piece of moist sponge over the tube is generally used, and is frequently changed. The tube must be kept clean from membrane and mucus by means of feathers, which should stand in a solution of carbonate of soda. The nurse must understand the use of the tube, so that in an emergency she could replace it,

or at the worst keep the tracheal incision open with her forceps till the doctor can arrive. The child must be regularly fed, kept dry and clean, and notice taken if there be any regurgitation of liquid through the nose.

Private Nursing. — This branch of the profession affects the general public more closely than any other, as both doctors and patients depend almost entirely on the trustworthiness and experience of the nurses; and yet it is the one most open to women of little or no pretensions to knowledge. That this is possible is due to the ignorance of the community at large, the apathy or mistaken kindness of medical men, and the cupidity of speculators. If women can be engaged at low salaries, with little or no investigation of their antecedents, and sent out as "trained nurses" at fees calculated to yield a handsome profit, who can wonder that things are as they are? The remedy lies in the hands of those whose work has called trained nurses into existence — the members of the medical profession. As long as they accept such arrangements so long only will they continue.

If every medical man would but ask a few leading questions of the nurse supplied to him from an institution, concerning her length of training, where obtained, her experience of cases similar to the one in hand, her method of carrying out certain orders, meeting any emergency that may arise, etc., semi-trained incapable women would be detected. No feelings of pity or wish to avoid trouble should be allowed to screen an incompetent, unsatisfactory nurse. The issues involved are too great, and nursing is too responsible a calling to be placed in prentice or untrustworthy hands; neither for sentiment nor economy, both equally false, should life be endangered or unnecessary pain and discomfort inflicted.

The manner and dress of a nurse serve as guides to the thoroughness of her training. A woman who is scrupulously neat, in a suitable inconspicuous uniform, businesslike in manner, yet bright and pleasant, who takes her orders quietly yet intelligently, and who keeps strictly to her own position, is likely to be suitable. Nurses need a "professional" manner as much as physicians, and the latter would add to the dignity of both professions by recognising and encouraging the fact. Flippancy and familiarity are especially unworthy of those whose work involves such grave responsibilities. Mutual respect is the groundwork of the confidence which must exist if the patient is to receive the full benefit of the treatment. The medical man must feel able to trust the nurse's ability and trustworthiness in carrying out his instructions to the smallest detail; and the nurse must prove herself deserving of such trust, and add to her other duties an absolute loyalty towards the doctor. By her manner of obeying orders she can also inspire the patient with wholesome confidence. If at any time the nurse cannot be present at the doctor's visit, a *written report* must be left for him, and his orders for her should also be in writing so as to avoid any misunderstanding. Orders should be given directly to the nurse, not through the friends; and care taken that she really understands them.

Her report also should be given to the medical man, if necessary before he sees the patient, or after, if not desirable in the sick-room.

The nurse should never take the friends into confidence about the case, nor express her own opinion to them. Infinite harm is done in this way, and often remarks are quoted to the medical attendant in a different manner from that in which they were originally spoken.

The vice of gossiping is a very grave one, and unfits a nurse for her office almost as much as the vice of intemperance. If a woman persist in thus offending she should not be employed. Criticism of the medical treatment, suggestions of further advice, or even of a change of the medical man, should never be tolerated; such behaviour is unconscientious in the highest degree, opens the door to suspicions of touting for special doctors, and might lead to the gravest results to the patient. If a nurse cannot conscientiously continue to work for a certain medical man she must have the courage of her convictions, and leave the case without reflecting on him in any way.

When sending for a nurse the medical attendant can do much to put her on a right footing with the household she is to enter. Too often training is supposed to render a nurse indifferent to sleep, exercise, or regular food. It should be clearly explained that eight continuous hours for sleep, at least one hour for exercise, and time for each meal, are necessary as a rule, though a good nurse will make exceptional efforts in case of emergency. Her meals should not be served in the sick-room; and if on night duty, her bedroom should be in a quiet part of the house. Necessary sleep and exercise are essential to keep a nurse fit for the duties and responsibilities which devolve upon her. The medical attendant generally knows something of the household, and can give the nurse some valuable hints which may enable her to avoid friction.

A private nurse needs special neatness and refinement, so as to keep both the patient and his surroundings in pleasant order. The toilet of the patient calls for scrupulous nicety; nails, hair, etc., being carefully attended to. The housemaid's work will depend upon the domestic arrangements, and is generally done by a servant, but the nurse is responsible for the room being in order. She can do much to comfort her patient by avoiding all unnecessary noise in remaking the fire (using housemaid's gloves to lift the coal, which should be in lumps); shading his eyes from too strong light, either from lamp or window; arranging flowers; finding out any particular like or dislike, and if possible attending to it; avoiding all whispered conversations, creaking doors or windows, flapping blinds, creaking shoes, rustling or rattling dress or ornaments, not shaking the bed in passing, in fact, feeling with as well as for the patient. When her services are not needed the nurse is better out of the patient's sight, though close at hand; and this is especially desirable if the nurse be reading to herself as in some long watches she may lest she sleep. Needlework, however, is never resented by a patient. A nurse should invariably wear her uniform when on duty whether by day or night.

Much depends on the way in which the nourishment is presented as to whether the patient will take it or not. This is entirely the nurse's province, and she should have a sufficient knowledge of sick cookery to supply any deficiency in this respect in the household. Everything should be served as daintily as possible, glasses, spoons, etc., perfectly clean and polished, clean tray-cloth, if possible a few flowers, small portions, and any particular fancy as to sweetness, etc., remembered. Every particle of fat should be removed from broths and beef tea, toast should be thin and crisp, bread and butter thin and lightly spread, nothing spilled on plate or saucer. The patient should not be told as a rule what is coming, as an unexpected thing is often more readily taken. Rigid punctuality is necessary, nothing spoils an invalid's appetite like delay. No stimulant should ever be given or allowed to be given without direct medical orders, and the kind and quantity must be entered in the diary. Food should never be tasted or cooled by being blown upon, it disgusts the patient. Food should never be kept in the sick-room, and plates, glasses, etc., are to be removed as soon as possible. Ice may be kept much longer if wrapped in flannel and placed on a colander to let the water drain away.

A private nurse needs great tact in so dealing with the friends and relations that orders may be carried out without offending them. If in any difficulty they will not yield to her persuasions she must appeal to the doctor for advice. Thoughtfulness for their natural feelings, and also for the household arrangements, so as to avoid giving unnecessary trouble, will do much to promote friendly relations. The present system of private nursing leaves much to be desired, but valuable reforms can only be obtained by those most interested, the medical men themselves. The nurses are too often isolated units, without a centre or standard, and so are apt to put themselves before the needs of patient or doctor. After their time of training and agreement is over they are inclined to think they know all that is necessary; they have no system on which to arrange their work, and unless they are specially fortunate no one to give aid or advice. Half the troubles that occur are due to inexperience in adapting themselves to the altered conditions in which they have to work; and it needs both tact and disciplined training to enable them to adjust themselves satisfactorily to the new circumstances.

Those interested in nurses as a class may give material help to individuals by advising and helping them in habits of thrift. The Royal Pension Fund for trained nurses and similar schemes offer unusual advantages for old age pensions, sick pay, etc., and grateful patients may do much for the nurses by helping them to become members of such associations.

District Nursing. — Nursing the sick poor in their own homes is now a recognised branch of the profession, though it is not equally realised that this work requires specially trained women. The cases are as varied and critical as any to be met with in hospital or private work,

with none of their favourable surroundings. In many places, manufacturing centres for instance, where the population has rapidly outgrown the hospital accommodation, or in scattered country districts, where the nearest hospital or infirmary may be many miles distant, the most serious cases must perforce be nursed at home. There are innumerable instances where removal would probably cause a fatal termination to the illness, and is only attempted as a lesser evil than leaving the patient to suffer untended. If a parent, especially the mother, is removed to hospital, the whole family may be broken up, and the worst moral results ensue. Where there are young children, also, the anxiety about them in her absence is a serious drawback to the mother's recovery. There are also many cases unsuitable for hospital, such as chronic rheumatism, paralysis, cancer, phthisis, children with hip and spine disease, etc., who can perfectly well be attended in their own homes by a trained nurse. It has a good moral effect in many cases for children thus to support aged parents, or for brothers and sisters to keep a delicate member of the family at home, instead of sending them into the poor-law infirmaries at the expense of the ratepayers. Therefore a district nurse needs full hospital experience if she is to carry out medical orders efficiently; and in addition she requires special training to meet the difficulties of the work.

Ignorance, prejudice, dirt, foul air, and often the want of the commonest necessaries, have all to be met; and nursing knowledge alone is of little value if it cannot be used to the best advantage under the circumstances. Still less can a woman who has only given three or six months' time to acquire both nursing and district experience prove a satisfactory district nurse.

The method of work usually accepted is for the nurse to have a certain number of cases within reasonable distance under her care, which she visits once, twice, or even oftener, every day, taking entire charge of each patient with regard to washing, bed-making, changing linen, applying poultices, dressing wounds, etc. She also is responsible for the sick-room and all its appliances being kept as far as possible in a cleanly, tidy condition, and fresh and sweet. It has been objected that unless the nurse remain with the patient no real good can result from her attendance. But part of a district nurse's duty is to teach the friends the right way to wait upon the sick person. They are generally anxious to help, and a sensible man or woman can be educated to be an intelligent assistant who can be trusted to administer nourishment, medicine, etc., at the proper intervals between the nurse's visits. Too frequently some benevolent person, feeling the need of nursing in a special district, forms a committee, selects a nurse, and sets her to work without thinking it necessary to consult those most concerned, the medical men of the place. Even when they are consulted and their views considered, there is doubt as to how and where the nurse is to be procured; generally she is obtained by means of advertising, and even then a lay committee is apt to select an unskilled

or unsuitable worker, because the real needs of the work are not understood.

Good hospital training, two years at least, and six months' experience in a district home, should be the minimum standard. To put women with no more than six months' experience of nursing the sick, and often of limited education and intelligence, in the position of district nurse, is a form of cheap philanthropy that cannot be too strongly condemned. A half-trained woman is worse than one with no pretensions to knowledge, and to place such responsibility in her hands (too often because she asks less remuneration than a fully-trained nurse), is an injustice to her, the patients, and the doctor who attends them. However sensible and willing, no woman could attain in the time even sufficient practical dexterity to do the best for the cases, and for lack of the special training faults of inexperience must greatly limit her usefulness.

No nurse, however well trained, should ever be expected or allowed to treat or prescribe for any case whatever beyond rendering first aid in emergencies. She should never undertake the nursing of a case that is not under a medical man, nor initiate or alter any treatment without his direct orders or permission: as in private work, all suggestions, criticisms and discussions of his methods are utterly inexcusable. Gossip is, if possible, even a more fatal fault in district than in private work. Besides not talking of one patient to another, the nurse should be reticent concerning her cases to those above them in the social scale. The respectable poor resent their private affairs being made known to district visitors, committee ladies, etc., and a nurse who thus betrays confidence will lose all influence over her patients and their friends.

A district nurse is generally sent to cases by medical men, clergymen, district visitors, or the friends of the patient. If not sent by the medical man in charge of the case, it is more courteous for the nurse to ask his permission before beginning her work, though in an urgent case she might help the friends to carry out orders at her first visit, and then ascertain if he wishes her to continue. A *written daily report* should be left for the medical man, and in acute cases twice daily, or even oftener, with the record of temperature, pulse and respiration, action of bowels and bladder, amount of sleep, food, stimulants, etc. In chronic cases a written report once or twice a week may be sufficient, stating the general state of health, condition of wound, such as an ulcerated leg, etc. By thus keeping in full communication mistakes and misunderstandings are avoided. One rule would save many difficulties, viz., that both doctor and nurse *invariably* communicate in writing, never giving or receiving verbal messages from patients or their friends. By implicitly carrying out medical orders, and by exact obedience, she will impress the friends with the importance of following directions. The nurse must aim at being the friend, not the supplanter, of the wife or mother, who may resent a stranger's intrusion until experience teaches how much more can be done by skilled hands. It is generally much easier to put the

patient than the room in nursing order. But by degrees the most disorderly room can be rearranged, and whenever possible this should be done, not by the nurse personally, but by the friends acting on her advice. The lesson is more permanent if they realise themselves that they can make and keep things tidier and more orderly. They prefer themselves to put away the extra garments that have accumulated, to remove the family linen "airing" between the bed and mattress of the sick person, to clear out boxes, sacks, and other rubbish that may be under the bed. Still, if there be no one else available, the nurse must ensure cleanliness herself, for she is responsible that all the appliances and surroundings are in order. She must be prepared to extemporise many kinds of contrivances. If it be not possible to move the bed from a draughty position a screen can be made from a clothes-horse and the family shawl, if a quilt or blanket are not available; or the same garment may be fastened as a curtain on a clothes-line. A roll of newspaper or brown paper will convert a common kettle into a steam one for the time. A sheet of the latter material is an excellent substitute for mackintosh. A small teapot forms a good feeder, a chair can be converted into a bed-rest; in fact, a good district nurse is rarely nonplussed for ways and means.

A stock of necessary appliances, such as water-pillows (more generally useful than the large water-beds), mackintoshes, bedpans, etc., should be kept for lending; also sheets, bed-garments, etc. Flannel shirts, open down one side, are particularly useful for rheumatic cases. A free use of Keating's powder, carbolic acid, or Jeyes' fluid for bedsteads, floors, etc., with carbolic soap and turpentine are useful in diminishing insect life.

Except under special circumstances night duty is the exception for a busy district nurse, as it prevents the other work. Trustworthy women, working under orders, can generally be found to relieve the friends at night.

The nursing of infectious cases depends entirely upon the local medical men. Except in epidemics, scarlet fever, typhus, and small-pox are not usually attended by the nurse. With due precautions, most careful disinfection of hands, hair and instruments, and the use of separate sleeves and aprons, enteric fever, measles, whooping-cough, diphtheria, and erysipelas may be attended without risk to other patients. Care would necessarily have to be taken not to go straight to a child after visiting measles, nor to a surgical case when attending erysipelas; but ordinary chronic cases might easily be nursed at the same time, also acute rheumatism, pneumonia, etc.

Whatever may be the local attitude with regard to midwifery, it is most desirable that, although the nurse may possess the requisite training to act in that capacity, she should not do so except at the request of the medical men, when she must only attend a limited number of non-surgical cases, or in an emergency. But whenever possible she should act as monthly nurse under the medical men, and by their orders, visit-

ing the cases twice daily for seven days, and once daily for another week, taking the mother's temperature, pulse, etc., and keeping her absolutely clean; washing the baby, taking care of its eyes, etc., and, by inculcating cleanliness and uprooting traditional prejudices, help to lessen the mortality amongst mothers and infants so largely due to neglect at these times.

District nursing should be entirely distinct from any form of almsgiving. All relief should be obtained from the proper local sources, never given directly by the nurse. Also the work should be unsectarian if it is to reach those most in need of its help. When arranging for a district nurse in any locality it is helpful to obtain information from one of the established systems of this work. A nurse fully trained is supplied, with every detail of cost worked out, and definite rules on which she must act. She is bound to send a monthly report of her work, with full particulars, to headquarters, in addition to that furnished to the local committee; and she is visited and her work inspected at regular intervals from the centre. The same holds good for homes, only there the superintendent, herself a trained nurse, is held responsible for those working under her. No interference with local arrangements takes place under this scheme; it does but ensure a supply of properly-qualified women, and a uniform standard of work. Experience has also shown that refined, well-educated women exercise a stronger influence and produce better results than those drawn from the same class as the patients. One they instinctively recognise as their superior can do more in combating their prejudices than one who is rather inclined to share them.

Whenever possible it is well to make the people help to support the nurse, on the lines of a provident club. A monthly payment of 4d. for a family (or less if local wages are low), and a charge of ½d. or 1d. per head for those over fourteen years of age is conveniently spared, and is better than the giving of skilled labour for nothing. Cases in receipt of poor-law relief would not be expected to join such a club, but the guardians should contribute towards the nurses' fund.

Puerperal Nursing. — The fact needs wider recognition, that though the puerperal state is naturally a normal one calling for little beyond cleanliness and ordinary attention, yet from constitutional or accidental causes the gravest complications may arise, which require trained skill if the case is to be nursed successfully. Therefore maternity work should only be undertaken by women with general as well as special nursing knowledge. Even in the most straightforward case much depends upon the nurse to ensure a good recovery for the mother and a contented, well-cared-for infant. It is not possible for a woman unaccustomed to attending sick people or young children, ignorant of the rudiments of anatomy or physiology, and often of the simplest laws of hygiene, to become acquainted with all that is essential for a monthly nurse in three months, much less in six weeks, the time considered sufficient for this training in most of the lying-in hospitals and training schools.

It is often stated that the modern nurse falls short of her untrained predecessor in the management of infants after the first ten days. It cannot be otherwise if the nurse have not seen anything of a baby after the first fortnight, and is as much at a loss as the inexperienced mother in dealing with it. Then the child becomes the victim of the ignorant advice of zealous friends as to feeding, quack remedies for infantile ailments, etc., and the seeds are sown of rickets and other diseases for which medical aid is sought too late. The mere handling of mother and infant needs time and experience to do it well, and with comfort to the patient; and in the washing and bed-making of a lying-in woman great care is necessary to avoid exposure and risk of chill. Also it frequently happens that the doctor does not arrive until after delivery has taken place. The safety of mother and child depends then upon the nurse; fortunately, in the majority of cases, masterly inactivity carries her safely through. But a smattering of knowledge, or the audacity of inexperience, will often cause undue meddling, and injuries to both mother and infant may ensue.

The more highly trained the nurse, the less danger is there of her taking too much upon herself; she realises the risk, and is more willing to depend upon medical aid and instruction.

Absolute cleanliness is the secret of successful puerperal nursing. A nurse attending confinement cases should always wear dresses of washing material, and large white aprons and sleeves that will turn up above the elbows. She must be scrupulously clean in person, especially having her hands free from roughnesses and scratches, with short nails kept absolutely clean. Her hair should be frequently washed and neatly arranged. She should be quite free from any wounds or sores; many a case of puerperal septicæmia might have been traced to the unsuspected ulcerated leg of the old nurse in attendance.

The nurse's duty is to prepare the patient and bed, to have all in readiness for the infant, to wait upon the doctor, to put mother and child comfortably back to bed when all is over, and to nurse the case under the medical orders. It is advisable for her to ascertain beforehand if her patient has the necessary appliances, so as to avoid confusion at the time. The room should be bright and cheerful, as quiet as possible, not near any closet or sink, and easily ventilated. The bed should be in such a position that it can be approached on both sides. The fire should be lighted, plenty of hot and cold water in the room, two or three basins, a quart jug (in which to warm the forceps if needed), a slop pail, towels, napkins, infant's clothes, dressing for the cord, dusting powder, olive oil, threaded needles, thimble, safety pins, blunt-pointed scissors, linen thread ligatures, flannel receiver, antiseptic lubricant, flannel, plain soap, etc. If possible sanitary towels should be used for the patient; these can be inexpensively made of carbolised tow or oakum in butter muslin; but, if preferred, ordinary napkins may be wrung out of hot antiseptic lotion ($\frac{1}{20}$ carbolic or $\frac{1}{500}$ perchloride) and applied.

Brandy, hypodermic syringe, irrigator, Higginson's syringe, glass

nozzle, catheter, and a receiver for the placenta should be at hand. Glass catheters can readily be cleansed, but require very careful handling.

The nurse should recognise the stage of labour by the pains, the short "grinding" ones of the first being distinct from the propulsive "bearing down" ones of the second stage.

If the bowels have not been well relieved a small soap and water enema may be given in the first stage, especially if the membranes have not ruptured, which can be ascertained by external evidence. The patient should be desired to empty the bladder also at this stage, and if in accordance with the wishes of the medical attendant, a warm antiseptic douche (Condy, or $\frac{1}{4000}$ perchlor.) is often given; but this must not be done without permission. A glass nozzle (without a terminal hole) should be used, previously boiled and soaked in a disinfectant. It is well in any case to bathe the vulva with a warm antiseptic lotion, and creoline (℥j. to Oj.) is especially useful, as plenty of soap can be used with it, a desirable feature in district maternity cases.

The nurse should always thoroughly cleanse her hands with hot soap and water and nail brush, and then immerse them in "$\frac{1}{3000}$ perchlor." or "$\frac{1}{20}$ carbolic" before touching her patient, and it is well for her to keep a basin of antiseptic lotion at hand, so that she may dip her hands in it each time she attends to the case.

Preparation of Bed. — A convenient arrangement of the bed is made by spreading a mackintosh sheet over the mattress, covered by a blanket and under-sheet. In district cases sheets of strong brown paper will keep moisture from penetrating to the bed. Over the under-sheet another piece of mackintosh is laid, covering the lower half of the bed on the right side. This is covered by a small blanket, a folded sheet, and, if procurable, an accouchement sheet. In poor homes clean old quilts or any thick material can be used, over brown paper or an oilcloth table cover. The bed-hangings should also be moved from the side of the bed. The mackintosh, etc., may be kept in position by safety pins at each corner. The upper sheet, blankets, and quilt are folded back to the left side of the bed, ready to be replaced, and a sheet or small blanket, as preferred, is placed over the patient. A clean draw-sheet and the binder are rolled up and placed at the head of the bed, with six strong safety pins. A pulley is firmly fastened to the foot of the bed (an ordinary round towel is a useful one), and if necessary a piece of board or a flat stone is placed against the foot-rail for the patient's feet.

Toilet of Patient. — She is dressed in clean night-clothes turned up and secured on each shoulder by a safety pin. A couple of clean petticoats are worn, stockings without garters, and bedroom slippers, and a dressing-gown, which latter garment is removed and a shawl put across the shoulders when the patient has to lie in bed at the last.

Food. — Warm milk, tea, beef tea, etc., may be given from time to time — the last being a valuable stimulant to under-fed, ill-nourished

women. The nurse must be prepared for vomiting during the first stage of labour, and sometimes a shivering fit, without a notable rise of temperature, announces its termination.

Second Stage. — When the pains become decidedly propulsive, the patient must lie on her left side with her spine on a line with the edge of the bed, her head supported by a pillow or pillows, the knees flexed, and the feet pressing against the foot of the bed. The nurse can materially assist the patient in the second stage by supporting the lower part of the back during each pain. She may also be ordered to apply hot fomentations to the perinæum if there be rigidity; these consist of wool or flannel wrung out of hot antiseptic lotion, and must be frequently renewed. When the child is born the nurse will hand scissors and ligatures to the doctor, and if desired hold the uterus while the child is being separated. She has the flannel receiver ready warmed, in which she wraps up the infant, and puts it away in a warm place.

If animation be suspended, she must quickly prepare basins of hot and cold water, and help as directed with artificial respiration, rubbing with brandy, dipping into hot and cold water, etc. A small basin and pieces of wool will also be ready for the doctor to bathe the infant's eyes. After the expulsion of the placenta the nurse will take the orders of the doctor as to when the mother is to be made comfortable, generally after the child is dressed.

First Toilet of Infant. — The water for the infant's first bath must be from 90° to 95° F., the child is quickly soaped, placed in the water, and gently, yet firmly, rubbed to remove all the adherent deposit from its skin. It is carefully dried, especially in the folds of the skin. Until the meconium ceases, oiling the buttocks and thighs will be found useful. Before dressing the cord, the ligature must be carefully examined, and if not firm, or there be oozing, it must be retied; the genitals and anus should also be noticed in case of malformation. The cord may be wrapped in antiseptic gauze, and placed in a square of linen with a slit in the centre, through which it is drawn, and then neatly folded in; or it may be well powdered with a mixture of 1 part starch-powder, 1 boracic powder, and 1 oxide of zinc, and enveloped in the linen. This is kept in place by the flannel binder, which may be firmly, but not tightly applied. *No pins* must ever be used to fasten the several garments; they must be neatly sewn on, except the napkins, which are secured by a safety pin, and the ends of the long flannel, which are turned up over the feet, are similarly secured at each corner.

Toilet of Mother. — When the child is dressed, the mother, having rested, is made comfortable. The soiled skirts are drawn down over the feet and removed. A basin of hot disinfectant, $\frac{1}{4000}$, or creoline and water being ready, the vulva, thighs, and buttocks are thorough cleansed from every particle of discharge, well dried, and warm sanitary towels applied. The soiled draw-sheet and mackintosh are rolled tightly up against the patient, who turns towards the nurse, on to the clean draw-

sheet, also rolled close to her. The soiled sheet is drawn away, the other side of the patient washed and dried, the clean sheet spread out, and the patient turned gently on it. She lies on her back with the legs extended for the binder to be applied.

Application of Binder. — When this duty falls to the nurse, she puts the rolled-up strip of material, which is better than any shaped bands, under the patient, bringing one end across the abdomen, so that the end overlap on a line with the right hip. The lower edge should be well below the great trochanter, and the ends pulled tightly together, the left hand holding the under, the right hand the upper side, securing them by a strong safety pin. This is repeated until the whole abdomen is firmly bound, and at the fourth and last pin a fold is made in the under side of the binder to make it fit better, and it is left rather looser than lower down to avoid compressing the ribs.

Two people then gently lift the patient to the top of the bed; one raises the buttocks by grasping both sides of the draw-sheet, while the other raises the head and shoulders of the patient, and gently lifts her into position. Only one pillow is wanted at first. The draw-sheet and mackintosh may be pinned at each corner if desired, and an accouchement sheet placed under the patient. These are easily made, in the same way as sanitary towels for poor people, by placing carbolised tow or tenax between butter muslin. Or, if preferred, ordinary napkins may be wrung out of hot disinfectant lotion (say perchloride $\frac{1}{4000}$), and applied. The night-dress is unpinned from the shoulders, and drawn down, the covering blanket removed, the bed-clothes replaced, and the child given to its mother.

The **pulse** should be now taken, also the temperature; any rise over 100 in the pulse should be reported at once, and the nurse must be on her guard for hæmorrhage.

The **placenta** is placed in clean cold water for medical examination, and then is burned by the nurse.

Tidying of Room. — All soiled clothes must be removed from the room as soon as possible, and put to soak in cold water containing carbolic or other disinfectant. The room must be kept quiet, and the patient left to rest. Nourishment will be as medically ordered, but usually milk, egg and milk, or a cup of tea with much milk in it, are allowed almost at once. The nurse must obtain full medical instruction as to douches, use of the catheter, record of pulse and temperature, etc.

The room must be warm, but well ventilated, and the patient kept quiet for the first week.

After-Care of Mothers. — The mother must be kept scrupulously clean, the vulva being bathed at least twice daily, as after an action of the bowels. Douches will be given as ordered by the doctor — in every ordinary case the bed-pan, sanitary towels, sheets, night-dress, etc., should be warm when given to the patient.

The *nipples* must be well bathed and carefully dried before and after suckling and the breasts should be alternately relieved. If the nipples

become tender the doctor must be informed, as special applications, such as glycerine and tannin, eau de Cologne and water, etc., may be ordered, or a nipple shield. The child should never be allowed to go to sleep with the nipple in its mouth; this is a fruitful source of cracks and tenderness. If the breasts are very full and tense, with more milk than the child can take, they may be supported by a binder, and the medical attendant told, as the breast-pump may be needed. In district work one may be extemporised by filling a bottle with rather a wide neck with very hot water, emptying it quickly, and applying at once over the nipple — a soda-water bottle is very convenient for the purpose. If hardness still continue, hot fomentations and support should be applied until the doctor has seen the breast; the nurse must never use friction unless ordered to do so. The child may be put to the breast occasionally until lactation is established, usually on the third day. If it seem very hungry, a teaspoonful or two of milk and water, 1 to 4, warmed and sweetened, may be given. After the milk has come, the infant should be suckled every two hours during the day, and every four during the night, for the first fortnight or three weeks, gradually lengthening the intervals, especially at night.

Should a **mammary abscess** form the breast must be well supported; usually the patient's arm is fastened to her side. A convenient support, if poultices are ordered, is a square of linen with tapes at each corner, two of which tie round the waist, and the other two round the neck, holding up the breast. The square may be folded to fit the breast, and secured by a safety pin.

Light **diet** is usually given to the mother until the bowels have acted, and then ordinary digestible food. Stimulants are never to be given without orders. It is wise for her to avoid cheese, pickles, uncooked vegetables, etc., at any time while suckling, as they are apt to disagree with the child.

Torn Perinæum. — If the perinæum has been torn and stitched, the nurse may be desired to pass the catheter for some days, and this is most conveniently done as the patient lies on her side to avoid stretching the parts. The wound needs constant care to keep it as clean and dry as possible, the dressing being frequently changed. If douches are given the tube must not touch or rest upon the lacerated part. The binder should be put on as low as possible, and the knees tied together, the patient being kept strictly recumbent.

If allowed to micturate naturally it should be as the patient lies on her face, and the parts well bathed directly afterwards.

White Leg. — Should the patient complain of pain in the calf or thigh the leg must be kept perfectly quiet until the doctor comes. If the pain be severe hot wool may be applied, but no friction or movement of any kind attempted until orders are received for treatment. A cradle should be placed over the limb to take off the weight of the bed-clothes, and the patient must be moved as little as possible — special attention is to be paid to the back, ankles, etc., as sores are very

liable to form. The patient must never raise herself suddenly, or sit up while the leg is affected.

Should shortness of breath occur the doctor must be summoned at once, the patient kept as quiet as possible, and a stimulant given.

Should **septicæmia** arise, the nurse's duties are similar to those in a case of peritonitis. Any abdominal tenderness, offensive lochia, scanty flow of milk, or rise of temperature must be reported at once. A strict course of disinfection for the nurse, and for every garment taken by her into the house, must be carried out; and some weeks' interval must elapse before she attends another lying-in case.

The Infant. — Much depends upon the nurse in training an infant in regularity of feeding and sleeping, and, if well managed, both mother and child benefit. The baby should not sleep in the bed with the mother, but in a cot at the side; the heat may be maintained by hot bottles. Many infants are killed by suffocation among the poor for lack of this precaution. The *eyes* should be thoroughly cleansed every day with warm water; any redness or discharge must be at once reported, and the lotion ordered applied. A separate piece of wool or soft linen should be used for each eye, and burned at once; also the soft linen for cleansing the mouth and nostrils. The mouth should be washed after taking the breast. The *cord* is dressed daily, and, after it separates, a folded pad of linen and powder should be applied to the umbilicus for a few days. If the navel be inclined to protrude after the cord is off, the doctor may order a counter covered with lint or linen to be fastened over it with a strip of strapping two inches wide and four long, under the flannel binder.

Clothing. — The binders and the clothing should not be tight, as both digestion and circulation suffer, and the support to the umbilicus is insignificant. The mother should be advised not to dress her baby in gowns with low necks and short sleeves, but to keep its limbs covered.

The child is *bathed* (90° temperature) daily, though some prefer not to put it into the water until the cord separates. If the bowels and bladder are not relieved within twelve hours after birth the doctor must know. Often a hot bath will have the desired effect. After the stools become yellow in colour, any green motions, constipation, straining, or distension of the abdomen due to wind must be reported. Constant cleanliness and dryness are necessary, and care should be taken that the napkins are not washed in soda and water, as this chafes the skin. Any rash, sore, discharge, or persistent snuffling must be reported at once. If the child's breasts become tender and swollen, they must be protected from pressure by a piece of wool and shown to the doctor. The nurse must never squeeze or rub them.

In bringing up a child by hand the food will be ordered by the medical attendant, but the nurse must prepare it, and see it is always perfectly fresh, sweetened, and warm, and not given in too large quantities at a time.

The *bottles* must be scrupulously clean — the boat-shaped are the most convenient, also Timpe's (according to Prof. Escherich), which possess the advantage of having inscribed on the glass a scale of quantities to be prepared daily in proper proportions, and the amount for an infant's meals from three days old to twelve months. Other bottles can be kept clean with constant care. Two should always be in use: one, well scalded with hot soda and water, and rinsed in cold water, is left in boracic lotion until needed, when it is washed out with hot water before being used. The hole in the teat should not be too large, and tubes should be cleansed each time with a brush, though it is undesirable this kind of bottle should be used at all.

No stimulant or medicine should ever be administered without orders or permission. Warmth and dryness keep a child contented; many an attack of screaming attributed to "wind" is really due to cold feet. In obstinate flatulence dill water may be ordered, and a small teaspoonful of warmed olive oil, if given daily, prevents constipation.

A monthly nurse can do much by thoughtfulness to avoid giving additional trouble in the household.

In thus sketching the duties of modern trained nurses and their position as regards the medical profession, I would urge that more rather than less training and discipline is needed in every branch, and it is entirely in the hands of the medical men to raise and insist upon the maintenance of a high standard. Both callings would profit by it, and the sick of every rank in life would reap the benefit. In no other work are Browning's words so true —

> Oh, the little more, and how much it is —
> Oh, the little less, and what worlds away.

AMY HUGHES.

THE HYGIENE OF YOUTH

I. Introduction. — Efficiency for the accomplishment of the work of life is a result both of the character and direction of the training received, and of the physical and mental vigour to which that training has led. And, surveying the question from a practical point of view, it is obvious that greater "staying power" and less training is better than excessive training with consequent diminution of vigour.

Two-thirds of the period of youth are spent in the process of education, and in proportion to the care and thought expended by parents and teachers will growth and development reach their highest expression, or ill-health and disease result. I have no hesitation in saying, from a

wide experience, that a due amount of care has never yet been bestowed upon the young human being.

In the training of the young the individual must be regarded as a whole, so that mind may not be developed at the expense of body, or *vice versâ*, but a harmonious dual development secured.

In the process of education, which in its proper sense necessarily implies both physical and mental development, the teacher too frequently ignores the former factor. It is the physician's province to point out that education must not be pursued at the expense of physical welfare. Though his advice may be too generally ignored or contemned, he must yet insist that his office is to guide the schoolmaster in his duties so far as they concern the health of the pupils; nay, even in respect of the teaching itself — so disastrous is the assumption that teaching needs no technical training — less serious consequences would ensue to the young were the physician's advice more frequently sought and adopted.

The proper aim, therefore, of parents and teachers being the attainment of the highest development of mind and body, it must be impressed upon them in every way that this result is dependent upon an appropriate training in youth.

In order to secure the highest physical growth it is necessary that an approximately accurate estimate should be formed of each child's constitution. Those who should receive the most careful forethought are: —

1. Children who are delicate or sickly.

2. Children who have had an ailment which may recur under unfavourable circumstances.

3. Children who, though healthy as yet, come of an ailing or diseased stock, a stock in the offspring of which, as the physician knows, hereditary ailments and diseases are apt sooner or later to appear. If these children be surrounded by favourable conditions during the period of growth, the tendency to such disease might be eradicated or mitigated. Partly through ignorance, but mainly from pure thoughtlessness, parents flatter themselves that, as their children seem healthy during youth, they have escaped the parental tendency; whereas if they would but admit that these children are likely to be stamped with their own die, and set themselves diligently to counteract the hereditary taint, the children would often have to bless this wise forethought for a healthy manhood.

It is incumbent on parents to bear in mind what is so well expressed by Dr. John Harley, that "within certain limits the healthy body can accommodate itself with facility to considerable variations in the external conditions, and those are the delicate who cannot readily do this, and who, in the transition process, are liable to develop abnormal action, or, in other words, disease." To ignore such tendencies to disease may hamper the child throughout life, and bring misery not only to himself, but possibly again also to his descendants, by entailing disease and premature death, or, still worse, that deterioration of character which ill-health so often engenders.

TABLE showing the average and mean height and weight, and the annual rate of increase, of 7855 boys and men, between the ages of 10 and 30, of the *artisan* class — town population: —

Age last Birth-day.	Height, without Shoes.				Weight, including Clothes of 9 lbs.			
	Average.	Growth.	Mean.	Growth.	Average.	Growth.	Mean.	Growth.
	In.	In.	In.	In.	lbs.	lbs.	lbs.	lbs.
10	50·52	...	50·50	...	66·31	...	66·0	...
11	51·52	1·00	51·50	1·00	69·46	3·15	70·0	4·0
12	52·99	1·47	53·50	1·50	73·68	4·22	74·0	4·0
13	55·93	2·94	55·50	2·50	78·27	4·59	78·0	4·0
14	57·76	1·83	58·00	2·50	84·61	6·34	84·0	6·0
15	60·58	2·82	60·50	2·50	96·79	12·18	94·0	10·0
16	62·93	2·35	63·00	2·50	108·70	11·93	106·0	12·0
17	64·45	1·52	64·50	1·50	116·40	7·66	116·0	10·0
18	65·47	1·02	65·50	1·00	123·30	6·97	122·0	6·0
19	66·02	0·55	66·00	0·50	128·40	5·08	128·0	6·0
20	66·31	0·29	66·25	0·25	130·60	2·20	132·0	4·0
21	...	...	...	...	...	...	...	...
22	66·60	0·29	66·50	0·25	135·40	4·81	136·0	4·0
23–30	66·68	0·08	66·50	...	139·00	3·58	138·0	2·0

TABLE showing the average and mean height and weight, and the annual rate of increase, of 7709 boys and men, between the ages of 10 and 30 years, of the most favoured classes of the English population — public-school boys, naval and military cadets, medical and university students: —

Age last Birth-day.	Height, without Shoes.				Weight, including Clothes of 9 lbs.			
	Average.	Growth.	Mean.	Growth.	Average.	Growth.	Mean.	Growth.
	In.	In.	In.	In.	lbs.	lbs.	lbs.	lbs.
10	53·40	...	53·00	...	67·4	...	67·0	...
11	54·91	1·51	54·50	1·50	72·9	5·50	73·0	6·0
12	56·97	2·06	56·50	2·00	80·3	7·39	80·0	7·0
13	58·79	1·82	58·50	2·00	88·6	8·27	88·0	8·0
14	61·11	2·32	61·00	2·50	99·2	10·61	98·0	10·0
15	63·47	2·36	63·50	2·50	110·4	11·21	110·0	12·0
16	66·40	2·93	66·50	3·00	128·3	17·92	126·0	16·0
17	67·84	1·46	68·00	1·50	141·0	12·69	140·0	14·0
18	68·29	0·43	68·50	0·50	146·0	4·97	146·0	6·0
19	68·72	0·43	68·75	0·25	148·3	2·20	148·0	2·0
20	69·13	0·41	69·00	0·25	152·0	3·87	150·0	2·0
21	69·16	0·03	...	...	152·3	0·27	152·0	2·0
22	68·93	...	...	...	154·7	2·44	...	...
23	68·53	...	...	...	151·7	...	...	...
24	68·95	...	...	...	149·2	...	...	...
25–30	69·06	...	69·00	...	155·2	0·42	154·0	2·0

The *height and weight* should annually increase, not, it is true, with steady regularity, for in autumn and winter the advance is less than during spring and summer. But the weight always bears a certain definite ratio to the height.

In a child a constitutional disease is usually regarded as a necessary evil, and the parent never dreams that a rational readjustment of the circumstances in the light of modern preventive medicine might have prevented the mischief.

We should never forget that a vigorous manhood is the greatest of all blessings, and that the vestibule to its attainment is a healthy childhood; parents must be educated to understand that the highest and most acceptable endowment which they can bestow upon their children is good health, and *after* that, a sound education; these blessings by forethought and foresight may usually be obtained.

Health must depend largely upon two conditions:—

1. The inherent properties of each individual.
2. The environment in which the individual is reared.

Only so long as the individual organism is placed in its appropriate surroundings — *i.e.* grown on its proper soil — can we expect to produce typical health and strength. Failing these necessary conditions we can only anticipate imperfect growth, meagre health, an absence of robustness of character and manliness, the manifestation of early disease, and the absence of vigorous old age.

II. The Environment. — I would first point out the necessity, as far as possible, of bringing up the young in the country rather than in town; and in detached residences, rather than in the immense blocks which constitute some of our schools and asylums. Where parents reside in towns every effort should be made to arrange for education in the country; if this be impracticable, opportunity should be made for spending the vacations there. The importance of this condition has repeatedly impressed itself upon my notice, when I have been consulted about the children of persons in comfortable and even in affluent circumstances who (with apparent exemption from any hereditary delicacy in the family) enjoyed all the requisites for healthy growth except this; and who, being brought up in a town, or even in a "healthy suburb," continually suffered from tonsillitis, croup, bronchitis, persistent bronchial catarrh or pneumonia. As soon as they were removed to a school in the country their ailments ceased, education was uninterrupted, and healthy physical development succeeded. In the case of nervous diseases this difference of effect between town and country is still more marked.

Last summer, when I joined in the inspection of a Volunteer brigade of five battalions comprising more than 4000 men, I observed in passing through the ranks of the various "companies" that the difference in height, breadth and aspect between companies levied in the country and those mustered from towns was astounding. These facts are clearly exhibited in detail in the carefully-prepared tables of Mr. Charles Roberts, which should exercise a decided influence on the modes of rearing the young.

The air of town and country is, of course, originally the same in composition. But town air is rendered impure, not only by the absence

of sunlight, but, as it would seem, by the presence of some deleterious elements. Hence the exhilarating feeling of breathing fresh country air as a contrast to that of the town. But the utility of transferring children to the country vanishes if they are confined to day-rooms and bedrooms with so insufficient an extent of *cubic space* that air has to be rebreathed.

There is no habit more common, and none more deleterious and uncleanly, than that of living, working and sleeping in ill-ventilated rooms, and breathing and rebreathing the same air. It causes ill-health and deficient growth, from the imperfect working of the internal functions of the body; and renders the human being disposed to the attack of poisons from without. There can now be little doubt that these conditions pre-eminently favour the development of tubercle bacilli. The effect of pure and impure air on health and mortality, as recorded by Parkes, is strikingly shown in horses; for in them the question is more simple on account of the similarity in different times and places of food, water, exercise and treatment. Formerly, in the French army, the mortality of horses was enormous. Rossignol states that, previous to 1836, the mortality of the French cavalry horses varied from 180 to 197 per 1000 per annum. The enlargement of the stables — the increased quantity of the ration of air — reduced the loss in the next ten years to 68 per 1000.

It is sometimes stated that nurseries and schools need only be supplied with half the amount of air-space, on account of the size of the inmates. No greater mistake can be made. Children cannot thrive well without the purest air; like the young of all animals, they are peculiarly sensitive to pre-breathed air. Yet parents will take any trouble, and make any complaint, about the quality and the quantity of the food at schools, but show no concern about the ration of air provided. If they have to find fault with the appearance of their children on their return home for the vacation, they immediately throw the blame on the inferior quality or quantity of food. The truth is that, in a large proportion of cases, the pupils are compelled to live and work hard in insufficient air-space, and to sleep in still less. This has been repeatedly proved by the diminution of excessive mortality on the provision of more air. The active functions of children, together with their quicker breathing, necessarily produce more rapid tissue change. It was found by Voit, that during waking hours more carbonic acid in proportion is given off, while during sleep more oxygen is absorbed than carbonic acid eliminated. And in his eighth report to the Privy Council, 1865, Sir John Simon stated, "that even healthy children, in proportion to their respective bodily weights, are about twice as powerful as adults in deteriorating the air which they breathe."

Place. — The quality of the soil on which the child is reared is of paramount importance, especially in relation to the position of the *water-level.* It is well known that water lying stagnant on the surface of land is very inimical to health; but it is not so well recognised that

unhealthiness is also produced where the subsoil is loaded with stagnant water.

Drainage of Soil. — Efficient surface and subsoil drainage, so as to lower the water-level even a foot or two, may remove consumption and diarrhœa from an entire district, and produce so improved a state of health among the inhabitants that the development of germ life in them is largely prevented.

In the selection of residence for a *delicate child*, other things being equal, the nearer it is to the sea the more equable the climate; the farther from the sea the more is the climate one of extremes. Hence the child who requires a moist, equable climate, with warm winters and warm nights, should live at the sea-side, while those who need a more bracing air should reside inland. Children who possess that form of delicacy which renders them susceptible to *constant colds;* those having a hereditary tendency to *rheumatism, consumption, feeble circulation, neuralgia, kidney disease,* and other such misfortunes, might be saved much misery could they pass their period of youth in a dry, warm situation. It must constantly be borne in mind, that although consumption is a parasitic disease arising from the attack of tubercle bacilli, yet these bacilli only find a suitable soil for their propagation in certain constitutions, or in feeble states of constitution; a vigorous condition of health resists them.

Further, where insanity, or even an excitable nervous condition — which is often exemplified in hysteria only — is known to have occurred in members of the family, the child should be educated where he can be out of doors most of his time, on fine days, so that vigour of constitution may be produced, for in this development the brain itself largely participates. Such a child should not be allowed to work at night, or for any examination, until his brain is mature in its growth. Above all he should be taught that immorality in any form is especially detrimental to the stability of his brain.

It is also imperative that a child born with this hereditary disposition should be educated, from his earliest years to manhood, away from home, and apart from the management of his parents or any relatives who are tainted with the nervous constitution, in a place where a regular life will be maintained under watchful discipline, where all waywardness will be dealt with by a firm but kind hand, and where he will work and play with those of his own age who are more robust in health and in character. By such means the nervous tendency may be eradicated: yet these very children are too often kept at home, where they are petted and pampered, never thwarted or corrected lest the nervous condition should be induced, and where peevishness, ill-temper, and petty tyranny are allowed full sway. Such surroundings make a hotbed for the development of the tendencies which it is essential to check. In the case of girls, who spend so much time at home, and are disposed to a nervous habit, it is still more imperative that their education should be absolutely freed from the influence of such surroundings.

It is most mischievous to tamper with the *emotions* of the young, for they are so unstable during this period of life as to be certain to run into channels unforeseen and undesired. Even religious fervour, if excessive, is often perverted into the shape of sexual immorality. In youth the appetites, desires and passions awake, untempered by reason, uninstructed by experience, so that at no time of life is steadfast guidance and help more essential. Yet how few boys — and still fewer girls — receive the needful aid from their home training; a *policy of silence* is substituted with results frequently disastrous.

III. External Conditions. — As regards *clothing*, it must be borne in mind that the skin is our most important gland, and requires protection to enable it to do its duty, and to prevent its functions being arrested by sudden chills or other changes of temperature. In this country, where the temperature of the body is always higher than that of the atmosphere, the use of clothing is to prevent the waste of the heat of the body.

The skin regulates the temperature of the body by means of its blood-vessels, and these are dilated and contracted by their vaso-motor nerves, which turn on or shut off the blood as stopcocks regulate hot water pipes. The equability of the temperature of the body is regulated by a mechanism now well known to physiologists. The cooling power of a sweating skin is enormous, and the chill arising from clothes damp after exertion or getting wet are well known. But no one catches cold, or becomes chilled, from keeping on wet garments so long as he is warmly clad, *i.e.* so long as rapid evaporation or icing is prevented. A non-conductor should, therefore, be worn next to the skin, so that the changes of its temperature may not be too sudden. Wool of various thickness is the best covering of the skin in summer as well as in winter.

It should be remembered that the bodies of children are less capable of resisting heat and cold than of adults. But the worst of all clothing for children is *excessive* clothing. From time to time I see children who, being considered delicate, are burdened with an inordinate amount of clothing which increases their delicacy — their skin is never dry. By a reduction of the excessive clothing the "delicacy" often disappears. Clothing should keep the skin warm, but not moist except under active exertion. When moisture is perceptible on the skin under ordinary circumstances by night or day, the clothing is excessive and harm will result.

In this country the summer season should be well established before a change is made in the thickness of the underclothing; much illness is occasioned by a premature change suggested by a few warm days in April or May.

Much care should be given to keep the *feet* always warm, for neglect of this entails unnecessary ill-health often mistakenly attributed to inherent delicacy. I continually see children, and whole families too, who are always ailing, and are consequently described as very delicate; whose

"delicacy" comes indeed of the mother, but only in this that she does not know the value of warm, dry socks and thick boots. That the lack of these is the commonest cause of enlargement of the tonsils I feel sure, and I suspect that it is answerable for a large proportion of the cases of post-nasal growths.

The importance of warm feet in the maintenance of good health has so impressed itself upon the attention of a shrewd schoolmaster who has 125 boys under his care, that every boy is compelled daily, as soon as he has settled indoors, not only to change his boots, but also to put on a pair of dry socks. The *drying of damp boots* before rewearing them has not yet received the attention it deserves, and in very few schools are means provided for this purpose. The miseries and deformities (such as chilblains, ingrowing toe-nail, flat foot, anchylosed toes and corns) originating from out-grown and misfitting boots — boots never intended to fit the foot, but only to suit the fashion — I must not here discuss.

IV. Internal Conditions. — Next in importance to fresh air, sunshine, and locality in the nurture of the young, is the material — *food* — necessary to provide for existence and for growth and development. Without nourishment, appropriate in quantity and quality, bodily vigour is impossible, resistance to parasitic disease fails, internal maladies arise, or less specific general physical and mental deterioration are induced.

A large proportion of the sufferings of adult life arise from the inappropriate food and cooking and the hasty meals of adolescence. Sometimes the diet of youth is so nicely adjusted to its cost that illness is barely averted, while growth and development are frustrated. A more short-sighted policy, even financially, it is difficult to conceive; the cheapest policy, in the long run, for the rearing of youths, is to feed them well, so that they may be advantageously started for the attainment of the maximum of size and strength. If thus helped to reach a vigorous adult age greater and better work will be obtained from them, with more vigorous brain power, higher character, and less liability to special incapacities or deficient energies.

Again, *variety of food* is essential to efficient digestion and liveliness of disposition; monotony of diet seems to produce monotony of character, probably by way of some defect of nutrition.

The periodical use of the scales — say, once a month — would indicate to parents and teachers beyond all doubt whether the child was well cared for or gravely wronged. It would reveal errors in the mode of life, — such as inappropriate, insufficient or monotonous feeding, overwork, or over-exercise, — and would also direct earlier attention to the advent of disease. Periodically carried out it would show whether the natural standard of height to weight was being maintained.

In estimating the significance of the measure and scales, it must be remembered that most children grow by fits and starts; rapid growth requires great care, ample food, more rest, and little work, while on loss of weight work should be diminished or cease altogether. In some

schools such a record is already kept, and has been found to be of the greatest assistance to the teacher. For instance, should the measure and scales disclose that all the pupils are deficient in height and weight for their age, it will be evident that some radical defect of management exists; should they indicate that one child here and there is below the average, a reference to the height and weight chart on entrance to school might show the child to be the offspring of a diminutive stock; on the other hand, if the original height and weight were then normal, the evidence would be clear that the child had been working excessively, fed too sparingly (perhaps on account of a squeamish stomach), or that illness or disease was imminent.

On the other hand, it is quite conceivable that many schoolmasters and mistresses would dread the introduction of this system, since it would reveal the viciousness of many of the present methods of education and treatment, and would involve (if its indications were attended to) considerable thought and alteration in the administration.

No work should ever be imposed upon boys or girls without previous sustenance. Food first, work afterwards, should be the invariable maxim. To work before food probably implies that the material necessary for the performance of the work must be absorbed at the expense of the system and to the hindrance of bodily growth. The meals, therefore, should be wisely arranged: a substantial meat meal should be provided for breakfast and dinner, so that the heavy meals may be consumed before the principal morning and afternoon work commences; lighter meals may be taken in the after part of the day when the heavy work is ended. On the other hand, a meat meal three times a day is objectionable and injudicious on all grounds, although I continually hear of physicians recommending this plan in the rearing of youth: it would be found most inappropriate for schools at all events.

The *cooking* of food for the young has scarcely received the attention it deserves and requires; this neglect and the supplementary stuffings at tuck shops are a fertile source of feeble health, meagre work, bad temper, and permanent damage to the digestive organs.

Insufficient *time*, again, is rarely allowed to the young for efficient mastication and saturation of the food with the secretion of the salivary glands. If a child abstain, for any reason, from eating a meal or meals, he must not be expected to perform his tasks as usual. Every child who does not eat his food should be reported to his master, careful inquiry made into the cause, and the omission repaired. It must never be forgotten that it is during the years of growth that the delicate child may overcome its feebleness and be made permanently strong, or the strong child be weakened and stunted.

I would especially point out the necessity of children being taught to use their *teeth* for the purposes of mastication, rather than be allowed the too frequent use of the knife, or be provided with soft foods; in this way only will the teeth be kept serviceable. Twice a year at least children's mouths should be inspected by the dentist.

Concerning the suitable *kinds of food* for youth, I would insist that *meat* should be provided twice a day, at breakfast and at dinner; that the crust of *bread* is more suitable than the crumb, and whole meal than white bread; that *porridge* is an invaluable article of diet; that *sugar*, so frequently denied, is an indispensable requirement, forming as it does their main heat-forming food, as well as the most important factor in the growth and work of muscles; that *milk* should take the place of tea and coffee; and that young people are better without *alcohol* during this period of life.

Food implies *waste*, which results from wear and tear, and is removed from the body by certain excretory organs. These products of combustion must be continually removed if health is to be maintained. As Dr. Lauder Brunton says: "As a rule, people are now fully alive to the risks they run from poisoning by sewer gas, or to put it more widely, from poisoning by products of decomposition *outside* the body; but perhaps we do not all of us keep so clearly before us as we ought the fact that *inside* the body there are all the conditions for the formation of putrefactive products, and the most favourable arrangement for their rapid absorption." The need of the daily removal of these products from the body is not yet sufficiently taught and enforced in the young, and as a consequence much unnecessary ill-health ensues, and the appearance of piles is facilitated and encouraged.

V. As we have discussed the suitable environment for the human body during early life and also the material necessary for growth, we must now consider the purport of this care, and we shall find that the highest attainable development is impossible without the *exercise* of functions.

As unused organs atrophy, it is, therefore, essential that they be employed in order to ensure a maximum of growth and usefulness. But it must be borne in mind that whether we consider the exercise of the brain which, during this period of life we shall term *work* or *education*, or the exercise of the body, which we shall term *play* or *recreation*, exercise increases growth, while over-exercise stunts it. This is doubly true when we are discussing immature but growing organs; for strain of any description is detrimental to their efficiency. And exercise of function is not only essential to growth and development, but also to the healthy maintenance of the brain and body when normal growth is attained. In the performance of work energy is expended and finally exhausted; and this end comes sooner in the young than in those whose tissues are matured. Moreover, the young have to tread unbeaten tracks, which consumes more force than the pursuit of more or less accustomed studies. This opening up of new ground necessitates exertion, and unless the exertion is put forth with pleasure, it is apt to become harmful; whereas information acquired by the young with pleasure rarely occasions injury. Hence the importance of the study of "likes and dislikes," and of fostering work for which the pupil shows a taste, slowly adding that which is at first distasteful. In fact, the appetite for work is very similar to the appetite of eating; the child will not only thrive, but get

fat on that which it likes, while it will eat so sparingly of what is distasteful that the body will suffer. It is true of mind as well as of body, if unsophisticated, that we all like what we can readily digest. Moreover, as variety of food is essential for the adequate development of the body, so variety of work is imperative for due development and nourishment of the brain; and as slow and regular development of the body produces the finest and most permanent results in strength and durability of other tissues, so it is also with the brain itself.

The prime duty of the teacher is to develop whatsoever faculties a pupil has, however rudimentary they may be; and he alone is the real educator who knows how to compass this, instead of passing all pupils, like corn, through the same mill. Every faculty thus developed becomes a stepping-stone in educating other faculties which may be still dormant; though sometimes special ability in one direction may coexist with utter incapacity in others, mentally and morally. It is natural to all children to desire knowledge, — a desire which, unfortunately, our teachers too often succeed in extinguishing outright.

The true aim of training and of education should be to develop the best type of manhood in mental, moral, and physical well-being, — an aim, I regret to say, too frequently disregarded, especially in the training of girls, who should receive the greater consideration on account of the peculiarity of their growth and the demands to be made upon them in early motherhood. The young are allowed insufficient time for sleep; they are often deprived of fresh air and exercise by faulty school regulations, or unwisely-assigned punishments; they have little time to masticate their food owing to the hurry of school customs; and their hours of work are usually too prolonged, extending throughout the evening and too far into the night, to permit either of good work or a healthy development of the brain. An intimate friend of mine, and a born educator of the young, has informed me that since he abolished evening preparation of work in his school of considerably over a hundred young boys, not one case of sleep-walking has occurred, although many cases happened before this reform.

The worst feature in this prevalent method of education is that the long hours and clumsy educational methods compel the work to be performed under a sense of fatigue, so that the work itself is not of lasting value, and the brain may be damaged in the process. These imperfect methods of education are likely to continue until teachers receive a technical training in their duties, or at any rate till they cease to despise and abhor it. The education of the youth of the upper and middle classes in England is the only business for which a man is not trained.

The successful educator considers his pupil as a whole; it is the disregard of this unity that leads to harmful results. Each child possesses but its own proportionate stamina and mental ability, inherited and acquired. The ability may exist potentially in abundance, but of what avail unless the stamina be sufficient to provide a plentiful supply of good red blood for the sustenance of the brain. This brain nourish-

ment is the product of an efficient digestion of food, appropriate in quantity and quality, of *fresh air* and *exercise*, and of ample *sleep*, for the nutrition of the brain takes place mainly during sleep.

In the regulation of the *hours of work* will any sane man uphold the invariable custom which prevails of assigning the same number of hours of work to a young child when he enters school and to a senior pupil at the point of leaving? It would be as reasonable to expect him to undertake work of a similar order of difficulty. To some extent it is recognised that one of the chief functions of the competent educator is to graduate the training of the brain from short and easy tasks to more rigorous and strenuous exercise; but the length of the hours of work should be similarly gauged, as the young are without that power of sustained endurance, which comes only with the completion of education. If sterling and lasting work is to be accomplished during youth, and the brain is to be benefited in the process, teachers must learn that the work of the immature brain must be proportioned in difficulty and duration to its age and capacity. Yet the work assigned is sometimes so disproportionately severe that progress is arrested, or, too often, converted into retrogression; at other times the work is too prolonged, and tells its tale in weakened brain, body and interest; the character also suffers, in consequence of the temptation to employ illegitimate means for its accomplishment, or to avoid punishment on account of failure. A *scale of work* should be adapted to each age; and this again will require revision and remission in certain cases and under special circumstances of age and sex. In this scale should also be included any work assigned as punishment.

TABLE OF THE SCALE OF WORK.

Ages.	Hours of work per week.
From 5 to 6	6
,, 6 ,, 7	9
,, 7 ,, 8	12
,, 8 ,, 10	15
,, 10 ,, 12	20
,, 12 ,, 14	25
,, 14 ,, 15	30
,, 15 ,, 16	35
,, 16 ,, 17	40
,, 17 ,, 18	45
,, 18 ,, 19	50

Each faculty of the brain — such as thought, memory, special sense, muscular co-ordination, and other functions — requires its own special stimulation for purposes of development. Every brain has its natural high-water mark of effort and capacity. The systemic circulation of the blood affects the central circulation so intimately that on it depend not only the growth of the brain itself, but its functions also during the process — a full circulation aiding a flow of ideas and the retention of facts. The debility of more rapid growth — occasionally seen in boys, and habitually in girls — like that ensuing on illness, causes a feebleness

of circulation, and in consequence apathy and incapacity for mental exertion, however eager the pupil may previously have been in the acquisition of knowledge.

The *quality of the blood*, like feebleness of circulation, dulls the mental faculties, as in anæmia, whether arising from deficient food, loss of blood or overwork. No less injurious are the *impurities* which may circulate in the blood, and so irritate the brain matter as to give rise to all the symptoms of overwork, as is seen in the case of constipation, biliousness, albuminuria and so forth. It is, therefore, manifest that brain capacity, although in part it depends upon progenitors, depends also in part on environment. The bounds of safety can easily be overstepped where graduation of the amount and difficulty of work is not provided for.

It is not always the bright and promising pupil, but frequently the dull, feeble, but conscientious one who is overpressed. Moreover there are grades of overwork, from poor health and loss of weight to a complete and often permanent breakdown; here it is that the scales tell so genuine a tale. Loss of weight — and even a stationary weight — during the years of growth means overwork, underfeeding, incipient disease, or recent illness. Yet children, while suffering from illnesses or well-marked functional disturbances, are often kept fully at work as if in robust health.

The converse case is only too common, in which a brilliant pupil from too early pressure becomes a nonentity, with an impoverished and incompetent brain.

It is, consequently, incumbent on those who have the welfare of the young at heart to gauge the material with which they have to deal; and we repeat that it is essential for teachers to be adequately equipped with the requisite judgment, the necessary technical skill in teaching, the tact and force of disciplinarians, and a knowledge of the physiological factors concerned. The circulation of blood in the young brain is always in excess of that which exists when maturity has been attained, and thus provision is made for the more rapid repair and growth. Moreover, all mental work makes the blood-vessels distended and the brain hyperæmic. If during this period of life work be too prolonged, and this pressure too frequently repeated, the blood-vessels do not recover during the brief periods of rest. In this way the brain becomes congested, and œdema of the cerebral tissue follows with alteration of function, symptoms of headache, sluggishness and perversion of thoughts, absence of mind, irritability, inability to fix the attention, which may lead even to organic diseases of the brain of various kinds.

It behoves the physician of the present day, however, to be exceedingly cautious in suggesting to schoolmasters that a certain brain is incapable of bearing the strain imposed, for the demand for our public schools being greater than the supply, the unfortunate pupil who may only require, in order to enable him to compass his duties, a little consideration in easing or lessening his hours of work and increasing his sleep, may not receive the required sympathy, but may be told that if he

cannot keep in the running his place must be filled by another eager applicant; his future career may thus be compromised. The brain wastes in all illness, and this atrophy renders it totally unfit for work, or even for reading a difficult book for a considerable time. I have not yet succeeded in impressing upon parents and teachers that, so far as one can judge from the apathy exhibited in these cases, and the easily induced fatigue, as well as from observation of nature, the brain wastes in equal proportion to the waste of the body.

It must also be remembered that knocks on the head, to which boys are liable from various causes, may alter the nervous structure, possibly from bruising and minute ruptures, and that prolonged cessation from work should be enforced even when the blow may have been of a comparatively trivial nature. [*Vide* art. on "Concussion of the Brain."]

But overwork is yet more pernicious in its effects when the necessity of an ample allowance of *sleep* is not recognised. It is a well-established fact that more sleep is required for the formative than for the intellectual activity of the cerebral centres; yet what a record do our schools furnish in this respect! It must not be supposed that the deleterious effects of overwork during youth can be compensated by an additional amount of sleep, for nature will not permit a forced brain to rest — one of the most manifest symptoms of undue pressure being wakefulness. The over-exercise of the animal functions nature does not resent, for the more the muscles are used the more the brain will rest. Teachers should know that deficient sleep means stunted brain and body, and must not forget that it is only by graduated exercise of the mental faculties that the highest condition of brain development may be secured for work in after years. Yet the child on entering school is only allowed the same number of hours of sleep as the big boy who is leaving, whereas two hours more should be allotted as the following table shows: —

THE AMOUNT OF SLEEP REQUIRED DURING YOUTH.

Age.	Hours of sleep.
Under 10 years	11
,, 13 ,,	10½
,, 15 ,,	10
,, 17 ,,	9½
,, 19 ,,	9

But while the child's brain may be perfectly satisfied on this scale until the advent of puberty, yet for some time before and after that date, perhaps a year — when the growth is enormous, especially in the case of girls, and the development of new organs entails a severer stress upon the system — this amount is insufficient, as much more sleep is required for growth than for repair.

VI. The Exercise of the body is necessary to attain a maximum of growth and vigour. — But the brain can never attain its largest growth nor its highest quality of nervous tissue from the exercise simply

of its own functions, for it is dependent to a large extent upon the vigour of the body, which is the manufacturer of the material on which it lives. As I have already pointed out, the growth of the brain depends upon the condition of its blood-supply; and the condition of the blood is dependent upon the state of the circulation, respiration, and the muscular and digestive systems. Hence the importance to the young of sufficient exercise. This exercise should take the form of games or recreation, in which refreshment the brain participates, rather than the form of a set lesson in the hands of a gymnasium instructor or the drill sergeant. These latter modes of exercise are desirable enough, but they should be an addition to, rather than a substitute for *school games.*

Exercise during youth is excellent: games are invaluable. We, as a nation, owe our success chiefly to our mental and bodily vigour, — a vigour which is irrepressible, and dependent mainly upon the games of boyhood, which render possible our sports of manhood. What other nation would dream of playing football in India and polo in Burmah? The physical education of the young trains them in perception and judgment, as well as in adroitness and courage. Even yet, however, the influence of physical education on mental and moral growth is not sufficiently regarded, nor is it yet fully recognised that bodily and mental culture must be concurrent if the highest development is to be attained. The sportsman precedes the trader in new countries, and the trader the statesman. Their qualities can be developed in our school playing-fields: let them, therefore, be encouraged in every possible way. No question in the training of the young is of more general importance than the mode of occupying out-of-school hours. This freedom from work should be a period of cheerful recreation and constant lively occupation, otherwise it becomes a time of weariness and idle lounging, and the character and tone of the young must consequently deteriorate.

In physical exercise all the functions of the body are engaged; the circulation of the blood is quickened, more oxygen is inhaled, and the impurities of the blood are thereby oxygenated and destroyed, so that the excretory organs of the body may remove the detritus from the system. Observe the young boy who is keen in games, and compare his physical condition with that of the dawdler. Notice his healthy complexion, good wind, elastic gait, splendid muscles, increased stature, and sure promise of vigorous manhood. Consider, again, how boys' games tend to develop a well-balanced mind and character; how they instil, as nothing else can, glowing spirits from the robustness of health, quick response to calls of duty, frankness of disposition, good temper often under trying circumstances, love of justice and fair-play, self-reliance, endurance, confidence in comrades, desire to excel, quick judgment, aptness to act with others for the good of all, courage under pain or difficulties, self-control, and last, but not least, how they check morbid desires and sensations by the expenditure of superfluous energy, which ensures purity of life. If school games had no other salutary influence than that of affording a

wholesome topic of conversation in out-of-school hours, they would be worth the infinite trouble which should be bestowed upon them.

In the regulation of the games of the young, where healthy rivalry may, in the inexperienced, lead to excessive competition, I think the physician should have a voice. I would, therefore, suggest the following precautions which are reasonable, without the unnecessary fuss which pupil and teacher alike resent: —

1. The physical examination of all children when they first enter school. In this way only can the healthy be safely compelled to play all games.

2. The proper apportionment of exercise consequent on this examination, in order that the physically weak, diseased or deformed may be restricted to that exercise which is suitable to each. In this way only should any boy be excused from the ordinary school games.

3. The medical control of all severe exercise, so that even those who are physically fit to undergo it may not be permitted to do so without prior and suitable training for the prolonged exertion. It is excess of exercise, or exercise imprudently taken, which is so deleterious to those who are growing; exercise in proper measure promotes health and strength.

Exercise should be gradual in its increase, or harmful results may follow. Those who think that, because they have excelled at some exercise during one season they can resume it in the next season without fresh training, are likely to overstrain and injure themselves. If we do not, therefore, wish to hear of the dangers of rowing, of running, and of football, of the golf arm and of the tennis leg, the muscles necessary to these exercises must be trained by degrees at the commencement of each season. All muscles may be educated to any strain within reason, but unused muscles are unable to bear sudden or prolonged efforts.

Syncope in boys during exertion is usually attributed to exhaustion, but my experience has shown that, while it may in some cases be occasioned by the physiological condition of the heart and vascular system at puberty, or be due to a temporary dilation of the heart resulting from active physical exertion in an unfit state of body, it is more frequently toxæmic, the excreting organs being inadequate to the new and sudden call upon them.

Physical education requires as much forethought, method, and application as mental, whereas too much routine is involved in both.

For all games entailing exertion the player should be clothed in flannel, which should be changed immediately afterwards and dried; where this care is not observed, chills and even dangerous illnesses are apt to arise.

It is customary for the young to undergo *training* for boating and other athletic sports. The purpose of training is to place the body in such a condition as to enable it to perform the hardest physical work rapidly, or for a prolonged period; it is, in fact, to produce the highest possible state of health for hard physical work. The essence of training

is that the heart and lungs should become accustomed to sustained exertion, and this is effected by degrees.

In training to obtain good "wind," it is of the highest importance to avoid indigestion, for nothing more thoroughly defeats that end. Food, therefore, as I have said, should be eaten slowly and masticated thoroughly, and no food should be taken between meals. There is a fallacious opinion among all trainers, be they trainers of mankind or of horses, that to those under training the smallest quantity of fluid should be allowed; hence these persons often suffer from actual thirst. Many people do indeed drink more than is requisite to satisfy thirst, man being the only animal which resorts to this mischievous practice. It should be a rule with every one, in order that the highest condition of health may be attained, to take only a sufficiency of fluid, say from two to three pints daily, except in hot weather or under great exertion and sweating. Water sufficient to satisfy thirst should be freely allowed, but in small quantities at a time; thus the athlete never becomes actually thirsty, — for every ounce of fluid which leaves his body another is supplied in its place. Dry tissues and unnaturally thickened thirsty blood are unfit for the highest functional activity. To suffer thirst for minutes or hours, and then, when the exercise is over, to take, as many do, an excessive quantity of fluid, may well cause discomfort, take away appetite, and entail indigestion and loss of sleep.

Again, change of work and change of play are as important as variety in diet. At the present time the games of the young are too monotonous, and insufficient attention is paid to natural tastes and aversions. This is not the place to discuss the merits of the several games suitable for boys and girls during their growth; but I would point out that the exercise adapted to boys is also compatible with the health and physique of girls up to the age of puberty; after that age the games of girls should gradually pass year by year into exercise of a quieter character.

The exercise obtainable from games, as well as that from hand-culture, should be various, not only for the better development of bones and muscle, but also for the development of the brain itself, as every complex movement has its brain-centre, which, in its turn, is developed by the exercise of its functions; so that we want not only football, cricket, rowing and running, but in addition, walking, brook-jumping, high-jumping, skipping, swimming, skating, racquets, fives, lawn-tennis, la crosse, golf, hockey, baseball, wrestling, fencing, boxing, gymnastics, physical drill, cycling, rifle-corps drill, rifle-shooting, camping-out, workshops, natural history excursions, gardening, music and drawing. With such variety of exercise, and mountaineering, riding, shooting and fishing in the holidays, the brain and body will be formed as a complete and harmonious whole.

The physical education of girls is seriously neglected, and little or no attention is paid to their bodily development. Why do girls so frequently fail in health directly they undergo hard mental work, sometimes becoming incapacitated for life, physical wrecks, and the victims

of hysteria and other neuroses? Simply because they and their friends attempt the impossible. If we are to have the higher mental education in girls, of which they are quite capable without injury, they must not be pressed, as they are at present, during these years when their growth and development are enormous, viz., from 11 to 14, when they leap, as it were, from childhood to womanhood at a bound, for all their nervous force is expended in this direction. Teachers must not fail to recognise the difference in constitution between the boy and girl. Continual application to work from day to day, from week to week, and from month to month, should never be enforced on girls; nor should they even be allowed to make such efforts; cessation and rest at menstrual periods should not only be encouraged, but even enforced. Their mental education, again, must proceed *pari passu* with a thorough physical education, otherwise, with rare exceptions, it must end in failure; perhaps in serious or life-long misery. If in Great Britain we cannot yet manage both, let the mental education remain as it was, and the physical education be undertaken more completely, so that girls may by degrees be prepared for the higher intellectual education, and become better suited for their womanhood.

At the present time a girl's education is *effeminate*, whereas it should be *feminine*. Why has it been considered unladylike for girls at school to be allowed any other outdoor exercise than a formal walk in the street? There is no conceivable reason for this restriction. The lady who has the courage to break through the spell and establish a good school for girls, in which their physical education shall be as well organised as their intellectual and moral education, will deserve well of her country, and will carry out one of the greatest and most needed reforms of the age.

Girls are naturally more subject than boys to nervous excitement, but this could be more effectually restrained by a sounder physical development. Our girls are so often what they are — "nothing but nerves," or "nothing but emotions," ready to faint on any, or without any provocation — because they are suffering from their faulty training and conditions unnatural to them; these evils will disappear when girls are reared under a reasonable system.

The absence of daily, regular and sufficient exercise renders girls listless and apathetic, entails pallor and anæmia, constipation with its sallowness, foul breath, and depressed spirits, crooked and stooping backs, and knock-knee and flat foot with characteristically awkward gaits.

It should be the aim of parents and teachers to instil into girls' minds the fact that it is their duty to try to be physically strong, and to provide for its attainment by adequate means. They should be taught the necessity of being vigorous as well as graceful, and naturally, instead of artificially shapely. But this perfection of body can only be reached during the period of youth, and by physical exercise, which, duly regulated, promotes not only muscular development, but also a vigorous nervous tissue and brain capacity, and above all, that strength of character which curbs irregular nervous expenditure. I repeat, if girls are to

receive a higher culture their physical education must precede any increase in their mental education. Without this the process cannot be safely effected, for the mental powers are developed in woman at a high physiological cost, which her feminine organisation will not sustain without more or less profound injury if bodily vigour go not hand in hand with it. It is more essential for a nation to produce strong, vigorous offspring than to educate girls to the highest standard. By the highest physical education girls can be made strong, comely and well-proportioned; while by the highest mental education (without this physical basis) they may be made into "blue-stockings," or neurotics, or both together. By physical education I mean games and recreation which cheer and elate, not merely gymnastics and physical drill, which afford exercise without elation. These latter exercises are mainly for the sickly and deformed; and curative rather than animating. By physical exercise, too, I mean exercise taken out of doors; without this condition at least half of its value is lost. In wet weather dancing should be encouraged; graceful movements and carriage are only to be attained by means of well-developed springy muscles. Every educator of girls should feel disgraced by the lounging attitudes and awkward gaits which prevail at most girls' schools, with their lop-sided shoulders and crooked backs, for in these is manifest the vicious system of education in vogue. Symmetry is of paramount importance in women for ensuring the production of healthy offspring.

While I hold that, subject to the restrictions I have laid down, girls may safely receive a higher education than has hitherto been accorded to them, I would urge that their moral education is of more consequence to themselves and the nation than their purely intellectual development. With a physical education such as is their due, we should, almost in a generation, eradicate the neuroses and anæmia to which at present girls are so prone; in their place we should perceive more even spirits and more stability of character, and the aping of man would give way to a more dignified respect for the qualities of their own sex.

I trust I have made it manifest that to produce a sound human being, it is imperative that there should be a concurrent development of mind and of its physical basis during the period of youth. It is during these years only that we can educe faculties, form character, and invigorate the physical powers and functions. The school, where most of the years of youth are passed, is an epitome of the world at large, — a place in which to prepare the young, and not to unfit them, for their duties as men and women.

CLEMENT DUKES.

LIFE ASSURANCE

Life Assurance, although scarcely two centuries old, bids fair soon to embrace the whole civilised world.

The casualties of life have become matters of scientific prediction; what seemed to be "accidents" are seen to be less and less under the dominion of "chance," which, indeed, is but a word to express our ignorance of the laws in operation.

The likelihood that a confidential servant will betray his trust can be estimated and provided for with the same precision as the probability of the occurrence of a storm, a shipwreck, a murder, or a suicide.

The medical selection of lives was not attempted in the early days of life assurance. The first life assurance society, "The Amicable," was founded in 1706, and existed for years before a medical officer was appointed. The same premium was paid by each applicant, whatever his age or apparent health. He was, however, called upon to state on oath that he believed himself to be a good life.

In process of time it was found desirable to exclude manifestly unhealthy applicants. Hence the proposer was required to appear before the Board. Some directors were shrewd in their judgment as to the value of a life, but it soon became apparent that a medical inspection was required for the selection of "first-class lives." The first medical officer was appointed to the "Amicable" in 1855, and to the "Equitable" in 1858.

Besides the health, the age of the life to be assured needs consideration, and the duration of the term of the assurance.

The premium required being greater in proportion to the age or "expectancy of life," it is customary for the medical adviser, in estimating the necessary addition, to ask himself the question, "Will the applicant before me, now 30 years of age, live as long as a healthy man at 35, 40, 45, or 50?" If he considers that the "expectancy" of the invalid life before him is as good as that of a first-class life at 45, he advises the addition of fifteen years in estimating the annual premium.

Other questions, besides the medical selection of lives, call for the attention of the profession; although in the domain of the actuary they have intimate relations with medical and medico-legal science.

Term policies are issued for short or long periods, of days, months, or years; a life may be accepted for a "short term" when uninsurable for a long one. Some disabilities that prevent the acceptance of the life may, however, so greatly increase the danger of speedy death as to demand the refusal of the risk, even for a few weeks; this is especially the case if the "habits" are bad. The premium receivable for a short period being very small, the loss involved in the event of a claim occurring is so great that no ordinary addition to the premium would cover

the risk. In these cases a large premium, say 3 or 4 per cent, is sometimes suggested instead of the usual addition of years.

Contingent risks, or assurance payable only in the event of one person, generally young, dying in the lifetime of another, are rendered unduly dangerous to the office if the younger life is a seriously damaged life. A high extra rating may then be insufficient to cover the risk. Thus a "weedy" youth at 25, whose habits are uncertain, may be ineligible against a healthy life at 50, though insurable for life with an addition. The medical examiner thinks only of the case before him; the actuary reminds him that, whilst the loss on a particular case might be comparatively large, the greater number of the "contingent risks" are never heard of again by the doctor or by the Board; they become void by reason of the death of the older life, or are dropped, the assurance having been effected for temporary purposes.

Furthermore, the mortality among recently examined lives (say within five years) is less than the tabular rate; consequently, for all forms of assurance where the period (five years) forms a considerable portion of the risk, the calculated premium is slightly in excess of the true net premium, and the "loading" in contingent cases is usually heavy.

Issue risks are often affected when the "heir presumptive" wishes to raise money on his expectations, there being no "heir apparent;" also when it is desired to quash a trust in favour of children, a marriage having been childless. In such a case the risk to be considered is not so much of issue by the existing marriage as of the death of the wife and remarriage of the husband; the chief considerations being the health of the wife, and the prospect of the man marrying again late in life and having children. If the wife's health be uncertain, the prospects of a second fertile marriage by the man may be considerable.

The cause of sterility in the woman often needs consideration. If this be removable the risk, of course, is greatly enhanced. Sometimes the issue risk to be covered is not only the birth of an heir, but his attaining the age of 21. A variety of issue risks has been proposed in which the probability of a woman, known to be pregnant, giving birth to viable twins has to be considered. In certain families and with certain individuals the probability of twin births is enhanced.

Endowment assurances payable during life, say on reaching the age of 50, 55, or 60, have tended to modify the work of a medical examiner by increasing markedly the proportion of "first-class lives." A proposer having a shrewd, perhaps well-grounded suspicion that his life will be a short one, in his natural endeavour to pay as little as may be for his privileges, is likely to select a whole life "without profits" policy, rather than a short term endowment which would double the annual premiums.

It is on this account that the medical examiner should scrutinise with especial care the "without profits" whole life policies, and look with a favourable eye on the short term endowments.

Members of the medical profession, who feel that Life Assurance is a business of which they have some special knowledge, tend more and

more to regard endowment assurances as a safe and remunerative form of investment in which they can obtain 3, 4, or even 5 per cent compound interest on their yearly savings, besides the security of an ordinary life policy in case of premature death. A man æt. 25 may, for annual payments of £28, secure an endowment of £1000 which, on attaining the age of 60, amounts with bonus additions to about £2000. At æt. 35, his practice having increased, he may take out another policy for £2000 at an annual payment of £83, so that on reaching 60 (when perhaps his powers are waning and his professional income diminishing) he receives, say £5500, and has no further premiums to pay.

The claims on this class of assurance are exceedingly small. When any cause, hereditary or personal, leads to the anticipation that the life will not be prolonged much beyond æt. 60, although normally secure up to that time, it is becoming customary to advise "endowment" of such cases; thus, perhaps, the remarkable absence of claims in this class may be somewhat modified.

The relative duties of chief medical officer, medical referee, and medical attendant need definition.

It is undesirable that the **ordinary medical attendant** should act as medical examiner for an office, although occasionally there is no alternative. If he undertakes to report, and accepts the fee, he is bound to consider the interest of the office first, and that of his patient as of secondary importance; motives of personal friendship must not influence his report.

The **medical examiner** is the adviser retained by the office, and is bound to consider the interest of the office as paramount. He must not allow himself to be swayed by the arguments pressed upon him, often with undue insistence, by the "agent," whose interest it is to carry through business, however insecure. The facts which the agent will supply may be valuable, but are apt to be one-sided and to need discriminating interpretation.

In some offices, where the desire to get business is great, the actuary may also try to put undue pressure on the medical referee, who must then remember that he is responsible to the directors, and is bound to consider first the well-being of the office. Whilst it is the function of the agent, and in a measure also of the actuary, to "carry through" every proposal, it is for the doctor to separate the wheat from the chaff, and to refuse insecure lives.

When an agent finds it difficult to mould the medical examiner, he is apt to try to take the proposer to some medical friend whose opinion he can dominate; hence it is important not to accept the report of an unauthorised examiner without full and satisfactory explanation. A large number of bad lives are thus insured in offices which do not insist upon reports from a medical referee of their own selection.

In his **personal examination of an applicant** each medical man should follow the methods of diagnosis to which he is accustomed.

He should take note of the condition of the heart and great vessels,

the lungs, the kidneys, etc. He will probably learn much from the character of the pulse and cardiac rhythm, and still more from the aspect, the morale, and general physical condition.

Whilst taking pains to investigate the case and estimate exactly the probabilities of life, the medical examiner should avoid over-examination. Would-be insurers are frightened away by too elaborate an investigation and too exacting an air. It is not necessary in every case, as some morbidly conscientious tiros seem to think, to use sphygmograph, laryngoscope, ophthalmoscope, and so forth. When the office is represented by a competent and carefully selected medical adviser, the end sought is best obtained without insisting on the registration of pulse, respiration, temperature, and quality of heart and lung sounds in various situations. Such formal inquiries tend to draw away attention from essential points, and vitiate, if they do not destroy, the value of the report. Even if now and then an obscure point be missed the office gains on the whole by not exacting too minute an investigation asking too many questions.

An experienced medical man should not take very long in deciding "yes" or "no," and he should not look too critical or "difficile."

If he himself has to labour through an endless series of questions, many of them trivial (*e.g.* colour of hair and eyes), and nonsensical (*e.g.* "of what temperament is the applicant?"), he has little time or spirit left for forming an independent opinion, or for the exercise of that sagacious and comprehensive judgment which, after all, is the thing sought.

Some offices receive reports from medical men having little experience of assurance practice, as is seen by their conclusions which have little relation to the observations on which they are based. Thus cardiac imperfections or albuminuria are mentioned, and yet the case recommended at ordinary rates, or perhaps with an addition of three years: or a high loading is suggested with nothing in the body of the report to justify it, except perhaps hernia or doubtful family history.

Offices whose forms are filled up by all sorts and conditions of medical men may find it of use to try to obtain facts rather than inferences; but where competent men are selected to make the examination, the simpler the form the more valuable the report. The following simple forms have been proved by long experience to be useful ones. They give an opportunity for stating in order the points likely to be of most importance for the consideration of the chief medical officer.

If an application be made to the "medical attendant," Form No. 2 is suitable.

FORM A. No. 1

Questions

Name, residence, occupation, age.

Are you married? Have you visited the tropics, when, and for how long? Are you now in good health? Is your health generally good? What medical or surgical assistance have you required, and when?

Have you any reason to suspect yourself liable to any affection of throat, lungs, heart, or any other organ?

Do you know of any hereditary disease in your family, such as asthma, consumption, insanity, scrofula, cancer, or gout?

Family History

Father, mother, brothers, sisters, age if living; if dead, at what age and from what cause? Is your family a healthy one?

I declare foregoing particulars to be true (to the best of my knowledge and belief). Signature of proposer.

The medical officer is then requested to report the result of his examination and inquiries in the following form:—

Height and weight of applicant (about). State of lungs, as shown by physical examination. Hæmoptysis. State of heart (by physical examination). Pulse. Gout or rheumatism. Digestion and abdominal organs. Genito-urinary system.

As to habits, whether regular, temperate and healthy; occupation and pursuits, whether or not detrimental to health. If a woman, state of uterine functions.

Is there any other circumstance calling for remark?

From examination do you think he seems likely to live as long as any other person of his age, and do you recommend his life to be accepted?

If so, whether at ordinary rate?

If not, what addition to the age do you advise?

Signature of medical referee, address, qualification, date.

Form No. 2

Confidential. How long have you known Mr. —— ? Are you in the habit of seeing him frequently? For what diseases have you attended him?

When did you last see him professionally, and for what disease?

Has he to your knowledge ever had any serious illness for which he has been attended by any other medical man?

Has it come to your knowledge that any of his near relations have suffered from consumption or any other hereditary disease? State what you may know, or are able to ascertain, of the health and longevity of his parents and other near relations. Do you consider that he is now in good health, that his cerebral, thoracic, and abdominal organs are sound? If not, state in what respect they deviate from health.

Is he temperate in his habits? What are his pursuits, and are they detrimental to health?

Is his physical conformation such as is consistent with a fair average life? Is he likely to live as long as any healthy person of his age? Do you consider that on the whole his life is a first-class one? If not, state the grounds on which you form your opinion, and the addition you think should be made to his age to meet the extra risk.

A space is left for any "special question" which the actuary or chief medical officer should, from other information, deem important, and a space left for signature, qualifications, and date.

The medical examiner should secure a private interview, for in the presence of the agent, or of any friend or relation, people are apt to be less frank and unconstrained. The proposer should be placed as much as possible at ease, and the inquiries should be made with quietness, courtesy and deliberation. The proposer should realise that he must give honest answers to definite questions, which are neither impertinent nor inquisitorial.

Directors are rightly severe in refusing applicants found to be tricky and secretive; when a proposer is detected in making a false statement it is right to decline to accept him.

Life assurance should be an honourable transaction for mutual advantage, and an attempt to overreach should not be lightly passed over by either party.

Preparation for Medical Inspection. — Before venturing to appear for medical examination many candidates take a bath, visit the barber, attend to the tongue, the teeth, and sometimes consult their family doctor that "they may be put in order" and be prepared for the ordeal. They also avoid giving any information about family and personal history which might lead to an extra rating, and dexterously omit all incriminating details.

Tropical Rating. — The practice of applying an extra rating for residence in the tropics, whilst giving occasion to criticism on the part of those who disapprove of the imposts, has been found to work fairly on the whole.

The risk of death in the early years of tropical life is considerable; it should be also remembered that an extra payment is demanded only during residence in the tropics, and is taken off when the proposer returns to Europe, with health perhaps broken by tropical disease.

The habit of "rating-up" for tropical fever, ague, dysentery, etc. (those who come for assurance after living abroad), is also fully justified by experience, as also are the ratings for "active service in the field."

Ratings for **dangerous avocations** call for consideration, among these the most frequent are occupations connected with the drink trade. It is customary to add a 50 per cent extra to such cases, even if classed as "A 1" by the medical examiner; but it is probably wiser to follow the rule of the more cautious offices, and absolutely to decline to accept proposals in such cases.

Extra risks arising from hunting and other active sports, which occasionally lead to a broken neck or concussion of the brain, may be accepted at ordinary rates on the ground that the improved health and longevity secured by an active, open-air life will more than counterbalance the extra risk.

Details regarding the diagnosis and prognosis of well-defined diseases may be dispensed with, but there are various conditions of imperfect health more difficult to assess concerning which something must be now said.

Susceptibility to disease, whether catarrhal or zymotic, exhibited by the proposer or his family needs consideration.

Vulnerability means increased risk and therefore extra rating.

Obesity. — Among conditions which may not be classified as "disease," or even "impaired health," undue stoutness, or excessive weight in proportion to height, calls for consideration. If obesity do not directly shorten life, it greatly increases the risks from acute and chronic disease. When an effort is needed to meet some unexpected strain, a large extent of useless, cumbersome tissue, a fatty heart, loaded liver, restricted lung surface, or kidneys prone to disease, become powerful allies of any intercurrent disease in the assault upon life.

As soon as a man's weight increases much above the average weight (see table), and the abdominal girth exceeds the chest girth, an extra rating is called for. Weight alone, without consideration of the build, the size of the bones, the conditions of the muscles, etc., is not a sufficient guide. Where the muscles are flabby, the abdomen pendulous, exercise insufficient, and food excessive, these conditions are incompatible with prolonged health.

A man, æt. 40, who, since the age of 20, has steadily increased in weight and bulk, and finds his breathing short on exertion, should not be accepted without an addition of five years, even though in all other respects he may seem well. Experience has shown (see *Report on Invalid Lives*, Equity and Law Assurance Society) that cases rated upon the ground of "stoutness" have proved a very unfavourable class. Habits of excessive eating and drinking and insufficient exercise tend to shorten life, and the very obese must be declined, or accepted for short terms with high rating.

Leanness. — When the weight is markedly below the average careful investigation as to the cause is required. If loss of weight be progressive the risk is enhanced, and the necessity for an explanation of the cause essential. It may be an early indication of phthisis, diabetes, cancer, or other progressive disease in the organs of digestion and assimilation.

Table of Height and Weight

Feet	Inches	Stones	Lbs.	Feet	Inches	Stones	Lbs.
5	3	8	13	5	10	12	4
5	5	9	11	6	0	13	5
5	7	10	10	6	2	14	7
5	9	11	10	6	4	15	9

If due to unusual slimness this need not necessarily imply delicacy or vulnerability, for the thin and "wiry" are (proverbially) long lived, or at least have so great an aptitude of recovery from disease as to justify their acceptance without extra rating, if careful inquiry elicit nothing against the life.

Leanness associated with feeble physique calls for considerable "extra." A man, 5 ft. 7 in. in height (see table), whose weight is but 8 st. 10 lbs. instead of the normal 10 st. 10 lbs., is probably a better life

than a man of the same age who weighs 12 st. 10 lbs.; or a man, aet. 40 5 ft. 10 in. in height, weighing 10 st. 4 lbs., instead of the normal 12 st. 4 lbs., is a more favourable life — other things being equal — than if his weight were 14 st. 4 lbs.

Two stone above or below the normal need in neither case necessitate extra rating, but demand extra caution. Note should always be taken of such deviation, and if no explanation be forthcoming adequate ground exists for extra rating.

Heredity. — Longevity is hereditary in some families, as is premature death in others (see *Analysis of Peerage Mortality*, Sprague), and this without noticeable strength or feebleness of physique.

When a tendency exists in the line of both parents to any special disease the heredity is intensified, notably in phthisis, cancer and insanity. The mother's power of transmitting disease to sons, who form the majority of insured lives, is greater than that of the father.

As with phthisis, hereditary gout is manifested earlier than the acquired form. If a tendency to gout or asthma exist on both sides a considerable extra rating is called for; where cancer is doubly inherited it is safer to decline, or to require all premiums to be paid by the age of fifty. Where one parent only has suffered from gout, rheumatism, heart disease, diabetes or cancer, this may be overlooked if the case be otherwise unexceptionable.

An investigation into the life and health of grandparents, aunts, cousins, is usually supererogatory, but the medical referee may be often aided by such an inquiry; he should never omit to report on the brothers and sisters of the proposer.

Phthisis. — As one death in eight is attributed by the Registrar-General to this cause, its early detection is of primary import; and as the mortality from phthisis among assured lives is but eight per cent, it is evident that medical selection has proved of great value. Half the mortality from phthisis among the assured occurs before the age of 40, and three-quarters before 50. (A large proportion of proposers have passed the most dangerous years from 15 to 25.)

The occurrence of **hæmoptysis** needs careful consideration; if following strain, and there be no evidence of inheritance, of heart or lung defect, of wasting or constitutional disorders; and if the applicant have passed the age of 30, the life may be accepted with a slight addition. Where hereditary tendency exists, the chest is long and narrow, the weight light, and the pulse quick, the life should be refused. Indeed, the coexistence of hæmoptysis with a history of hereditary phthisis would call for refusal. Full consideration of physical signs, etc., will be found in other articles.

In insurance practice, where the opportunities for complete examination of a case are limited, it may not be easy to make a prognosis with adequate confidence to justify the acceptance of a life with serious organic disease; but *every life has its value* and, with advancing pathological knowledge, accurate clinical methods and acquaintance with the

natural history of disease, a prognosis may be made with sufficient precision to justify the acceptance of the risk. This is certainly the case with the varieties of *valvular disease of the heart*, and in some cases of chronic *fibroid change in the lung* the life may be assessed with equal confidence and accepted with extra rating for short periods, or under the "endowment" or "limited payment" system. In cases of this class, however, the chief medical officer would probably require to see the case himself, and would not recommend it to the acceptance of the Board on any second-hand information.

Emphysema, when associated with chronic or recurrent bronchitis, especially if any signs exist of commencing cardiac dilatation, must be refused. If a somewhat inelastic chest wall, a prominence of thoracic venules, and tendency to dyspnœa on exertion, alone mark the emphysematous tendency, or if only occasional asthmatic attacks are recorded, an extra rating will suffice. Liability to bronchial attacks, whether of gouty, syphilitic, or phthisical origin, renders the life precarious even for very short terms.

Pleurisy. — Where traces of pluerisy exist, if the proposer be young, and if family and personal history, aspect, pulse, etc., should point to a possible tubercular origin or complication, the case should be declined. If the evidence indicate no more than the local contraction consequent upon old pleurisy of non-constitutional origin, a small extra rating will suffice.

Heart Disease. — The diagnosis and prognosis of cardiac disorders are fully discussed in other places; I can only say here that cases in which indications of muscular failure exist are uninsurable. Where compensatory hypertrophy conceals all evidence of circulatory defect the case may be considered, and acceptance advised on condition that all premiums be paid before degenerative changes are likely to occur. Aortic disease is more perilous than mitral. Cases of mitral stenosis and aortic regurgitation can but seldom be accepted. Less, however, depends on the situation and character of the murmur than on the history and constitutional state.

Irregular action, with feebleness of impulse and confused rhythm, is of evil portent.

Intermission of the pulse and apex beat may not prove the existence of serious defects, but calls for close investigation, and often leads to the discovery of gouty, dyspeptic, or nervous disorder.

The rapid, nervous, palpitating "insurance heart," so constantly observed among candidates for life assurance, requires skill and experience for its estimation. The beat is so rapid, tumultuous, bouncing and diffused that it suggests the idea of serious disease, and may indeed mask organic defect. Its variability and manifest association with general nervous perturbation will generally enable the physician to assess its import at the first interview; if not, a second should be arranged. Some proposers faint when thus examined, and may justly be regarded as too unstable to be accepted as first-class lives. These are persons who

are morbidly sensitive to a refusal or an extra rating, and it is important by firmness and kindness of manner to give them confidence and self-reliance. A medical referee cannot be too careful to avoid causing distress or anxiety in an applicant, even if he be obliged to decline the proposal.

Gout. — The bearing of gout on life assurance is important. Experience proves that a high extra rating is necessary. Gout was regarded in the early days of life assurance as conducive to longevity. The free imbibition of port was followed by occasional explosions recurring for a quarter or perhaps half a century, and leading to no marked deterioration. In recent years the wide extent of gout, as a constitutional affection leading to heart, kidney, liver, and more general tissue change, has been recognised even when no joint affection has occurred. Gout, as we know it now, calls for rejection in a large number of instances; and an average addition of 20 to 25 per cent in cases recommended for acceptance.

It must be remembered, too, that while phthisis is a "diminishing risk," gout is an "increasing" one. The mortality from phthisis falls mainly in early manhood, whilst that from gout falls in the years when life assurances are most usual, namely, between 50 and 60.

The close relation often existing between gout and *intemperance* in eating and drinking must not be forgotten; and the extra rating applied for "gout" might in some cases be more accurately entered under the heading "habits."

No part of insurance medical practice calls for so much discrimination as this. Intemperance, often markedly hereditary, may show itself in occasional craving for drink or other forms of nerve excitement, and lead to early tissue degeneration; the man who indulges freely and continually because he is never drunk being in the greater danger. Tact to discern habits of life, and skill to interpret indications (which have been perhaps carefully masked), are essential here.

Among the indications are the hurried manner, loud voice, fœtid breath, bloodshot sallow eye, flushed face, red nose, tremulous cold damp hand, tremulous tongue (often clean, especially in women), engorged fauces, carelessness of dress, etc. Where such signs exist no laboured proof in "friends' reports," or in the statement of the applicant, must be allowed to shake the conclusion of the medical examiner. If he be thus beguiled into accepting a life he was disposed, on personal examination, to reject for "habits," he is nearly sure to hear of the case "as a claim" in a time distressingly short for his reputation and for the office. The evidence as to the "temperance, soberness, and chastity" of a suspected applicant must not always be estimated by the weight or volume of the letters supplied in "friends' reports"!

It is not customary to regard **hernia**, if a suitable truss is worn, as a reason for extra rating. Neither need **piles** nor **varicose veins** be so regarded, except in so far as they give evidence of hepatic engorgement.

A history of **fistula**, if connected with piles which have been cured,

does not call for surcharge; but when there is any evidence of phthisis or constitutional weakness the proposal should be declined.

History of **gonorrhœa** justifies an extra rating; even when not followed by stricture, etc., it often brings in its train prostatic and vesical troubles which shorten life.

Syphilis. — During the existence of this disease in any primary form the proposal must be postponed.

If any secondary symptoms exist in a quiescent state an addition of five or seven years is required. When these symptoms have been in abeyance for two or more years only the case is not eligible at ordinary rates; it should be rejected if any lesion of brain, spinal cord, artery, liver, lung or kidney have occurred.

Albuminuria, whether present or not at the time of examination, if connected with kidney disease, with gouty, rheumatic, or cardiac disorder, or excess in eating or drinking, must be declined.

If the albumin be reported after scarlet fever or exposure, and to have disappeared for years, the health being perfect, acceptance may be recommended. Where it has been known to exist for many years without detriment (such cases have fallen under my observation) the case may be accepted, as a case of mitral disease or emphysema might be accepted, with a high rating or for a short term. When a trace only is to be detected, after food, and recurring at intervals, after several examinations at sufficient intervals, and with full knowledge of the case, acceptance, with five, seven, or ten years added, may be advised.

Glycosuria, while it exists, should forbid the acceptance of the proposal. It is often, however, a temporary condition, and may leave no ill effects; unless manifestly due to some transient state it should be regarded as a ground for refusal, and in any case for addition. In every form of diabetes the risks are too great to justify acceptance. It must not be forgotten that some urines not containing sugar may nevertheless cause a turbidity with Fehling's solution.

In cases of ataxia, and other forms of paralysis of a central kind, refusal is called for. In cases of old infantile paralysis, in diphtheritic paralysis, and in facial paralysis, a moderate extra should suffice (three to five years).

Pregnancy. — Recently married ladies often insure for very large sums, and the risk during the first year of married life is great.

The mortality in first pregnancies is high (1 in 74, Matthews Duncan) and it is wise to defer a proposed insurance until after confinement. It is usual to charge a small 10s. per cent addition to the first premium for a multipara, 20s. for a primipara. If the age is above 30, and the risk thus enhanced, an addition of 30s. is often justly made.

Claims. — Certificates as to the cause of death should always be considered carefully by the medical officer, and it would be advantageous if a medical report on each claim could be forwarded to the referee upon whose report the life had been accepted. Information to the chief medical officer would become the common property of the medical

referees, whose experience would thereby be increased, as an autopsy is invaluable to the physician who had charge of the case during life.

The wording of the death certificate should be clear and definite. Thus syncope may refer only to the mode of death and have no bearing on the nature of disease. "Childbirth" may mean phthisis, and should be limited to fatal incidents immediately connected with confinement. "Gastritis" may be a term used to conceal death from intemperance or irritant poisoning. "Dropsy," without evidence of dependence on heart, kidney, liver, should not be allowed to pass without investigation.

If the disease certified as the cause of death existed prior to the completion of the assurance, a question arises as to the *bona fides* of the transaction. If the statements made can be proved false the claim could not be maintained.

As a matter of fact offices are most unwilling to refuse any claim; but they have and ought to exercise the power to refuse claims manifestly unjust.

E. Symes Thompson.

DIVISION II

FEVERS

PART I. — INSOLATION

PART II. — THE INFECTIONS

PART I

INSOLATION OR SUNSTROKE

Under the designation of sunstroke, heat-stroke, insolation, thermic fever, calenture, heat apoplexy, heat asphyxia, ictus solis, and other synonyms, a variety of morbid conditions, from the simplest to the gravest, are included. However these conditions may be modified by personal susceptibility, local surroundings and climatic influences, they are all essentially due to heat, and are the result of direct exposure to the rays of the sun or to a high atmospheric temperature in the shade.

Great heat may cause—

1. A state of exhaustion leading to syncope.

2. An overheating of the nervous centres, blood and tissues; with a tendency to produce vaso-motor paralysis, hyperpyrexia (thermic fever), and subsequent asphyxia through the action upon the respiratory centres. Therewith lesions may take place, such as cerebral tissue change and hæmorrhage, and meningitis in various degrees. The symptoms in such cases are varied, and depend upon the portions of the cerebro-spinal centres affected.

The effect of heat upon the human body in tropical climates or elsewhere is a subject of considerable importance and interest. Man, of all animals, possesses the greatest power of adapting himself to changes of climate and temperature, and maintaining health under them. His body, under favourable circumstances of climate, food and habits, has the power of maintaining an almost constant temperature under extremes of heat and cold. Vigorous healthy persons, who lead temperate and well-regulated lives, can tolerate a very much higher temperature than others not so conditioned; and the natives of tropical climates — especially the coloured races — can tolerate an amount of heat to which the European would succumb: even they, however, suffer at times if the heat rise above a certain point, and natives of India frequently die from "loo marna," hot wind stroke.

The action of heat is much influenced by the hygrometric condition of the atmosphere. A dry hot air is better tolerated than a moist one at a lower temperature, because it favours perspiration and keeps the body cool; while damp air diminishes evaporation and the refrigerating proc-

esses of the body. When, from any cause, perspiration fails, or the natural eliminative functions are interfered with, especially when the air temperature exceeds that of the normal heat of the body, suffering soon ensues, and danger from ardent fever or heat asphyxia becomes imminent. That these evil consequences are not due to the direct action of the sun alone is shown by the fact that many of the fatal cases take place in rooms, tents or hospitals, at night, or in the early hours of the morning before sunrise, especially if the air be vitiated as well as hot: previous disease, debility, or irregular and intemperate habits, dispose to insolation.

The effects of all the conditions of hot climates, including heat, are not yet sufficiently determined, and we must look for further information to medical men practising abroad. Continued exposure to great heat cannot long be endured, even by the healthy human body, with impunity. Parkes and others have shown its injurious effects on the nervous system, on secretion and elimination, and on the digestive and assimilative processes. It causes fever from the simplest to the most ardent form; and it is often combined with pernicious miasmatic poisoning, extreme cases of which may be confounded with or pass into the most aggravated forms of thermic fever or asphyxia.

Insolation generally takes place in the hottest months of the year. April, May, June, and July give the highest returns in India; but whenever the temperature is high enough in other countries the same results obtain. For example, it is very frequent in North America every year. In 1894 it proved very destructive in New York; and in 1892 many places in Europe suffered with a severity unsurpassed even in India or other tropical countries. Reports from Vienna in 1894 show many cases of heat-stroke; on the 25th of July twenty-seven people were conveyed to the hospitals.

It has been stated that sunstroke seldom, if ever, occurs at sea; but this is negatived by the records of the vessels passing through the Red Sea, Indian Ocean, Persian Gulf, and other tropical seas. I have myself witnessed death on board steamers in the Red Sea from insolation.

Maclean tells us, among other examples of insolation occurring on board ship, that Boudin relates that, while at Rio Janeiro, the French war-ship *Duquesne* (*Statistiques Médicales*) had 100 cases of insolation out of a crew of 600. Most of the men were attacked, not when exposed to the direct rays of the sun, but at night when in the recumbent position — that is, when breathing not only a hot and suffocating, but also an impure air.

M. Bassier, a French naval surgeon, gives an account of 18 cases out of a crew of 78 men, which happened on board the man-of-war brig *Le Lynx*, cruising off Cadiz in August 1823. The heat, aggravated by calms, was excessive — 33° to 35° C.; the vessel small and overcrowded.

It is hardly possible to fix any particular degree of external tempera-

ture as one of excessive danger, because, as before stated, the tolerance of heat is very great in persons in perfect health in a pure atmosphere, and also in the dark-skinned races; but, under the conditions before mentioned, the danger is great when the temperature is equal to or higher than that of the body. A temperature of 110° or 115° F. or higher, in very dry air in motion, would be better tolerated than one of 90° or 95° F. in an atmosphere laden with moisture; especially if it be vitiated, as in barracks or rooms, by human respiration, or telluric or other miasmata.

All who suffer do not die; some perfectly recover, but many are permanently injured, and made unfit for service in a hot climate, or even become permanent invalids at home.

In 1891 the numbers of the European army in India were 67,030. Of these there were 228 admissions from heat-stroke and 65 deaths.

In 1892 the numbers were 68,162. There were 223 admissions from heat-stroke and 61 deaths.

In 1891 there were 3137 women with the European army. Among these there were 2 admissions and 2 deaths from heat-stroke.

In 1892 there were 3101 women with the army, but no admissions for heat-stroke; one death out of hospital.

In 1891 there were 5886 children with the European army. There were 3 admissions and 2 deaths from heat-stroke.

In 1892 there were 5762 children with the army. There were 4 admissions and 4 deaths from heat-stroke.

The native army in 1891 numbered 128,600. There were 22 admissions and 12 deaths from heat-stroke.

In 1892 the native army numbered 145,340. There were 43 admissions and 18 deaths from heat-stroke.

In 1891 the jail population of India numbered 101,019. There were 77 admissions and 40 deaths from heat-stroke.

In 1892 the numbers were 103,159. There were 77 admissions and 41 deaths from heat-stroke.

The above numbers show that the admission-rate per mille from heat-stroke in the European army in India was, in 1891, 3·4; in 1892, 3·3; while the death-rate in 1891 was 0·97; in 1892, 0·90. Among the women with the European army the admission-rate in 1891 was 0·64; in 1892, 0; while the death-rate in 1891 was 0·64; in 1892, 0·32.[1] Among the children the admission-rate in 1891 was 0·5; in 1892, 0·7; while the death-rate in 1891 was 0·34; in 1892, 0·35. In the native army the admission-rate in 1891 was 0·2; in 1892, 0·3; while the death-rate in 1891 was 0·09; in 1892, 0·14. Among the jail population the admission-rate in 1891 was 0·8; in 1892, 0·7; while the death-rate in 1891 was 0·40; in 1892, 0·40.

The following statistics and tables are taken from the reports of the Sanitary Commissioner with the Government of India for 1891 and 1892:—

[1] The one death was out of hospital.

Deaths from Heat-stroke in the European Army in India in 1891 and 1892 at the different Ages.

Age.	1891.	1892.
24 and under . . .	35 or 1·06 per mille	26 or 0·76 per mille
25 to 29	14 or 0·58 ,,	21 or 0·84 ,,
30 to 34	8 or 1·41 ,,	9 or 1·65 ,,
35 and upwards . .	7 or 3·33 ,,	5 or 2·40 ,,

Deaths from Heat-stroke in the European Army in India in 1891 and 1892 at the different periods of Residence.

Length of Service.	1891.	1892.
First and second years .	36 or 1·74 per mille	23 or 1·00 per mille
Third to fifth year . .	18 or 0·59 ,,	22 or 0·72 ,,
Sixth to eighth year . .	5 or 0·43 ,,	12 or 1·03 ,,
Eleventh to fifteenth year	3 or 1·81 ,,	2 or 1·40 ,,
Fifteen years and upwards	2 or 3·27 ,,	2 or 3·85 ,,

The statistics show how the effects of heat influence a certain class of persons who are under hygienic control; reliable data thus being afforded on which to determine the value of this element of the death-rate of a certain section of the population whose vital statistics are trustworthy. In others less protected, as in the scattered European, Eurasian, and immense native population, the incidence of the disease is often greater. In seasons when there are great accessions and waves of heat all over the world the disease and the mortality from it increase. Such waves of high temperature recur at uncertain intervals. No doubt the same obtains in other countries where the climatic conditions are similar; it is needless, therefore, to produce further statistics, as these sufficiently illustrate the subject.

A number of cases of hemiplegia are reported by the Sanitary Commissioner with the Government of India, which there is reason to believe were also due to attacks of insolation; but as it is not certain that all were so caused, I am content to allude to it generally as one of the possible results of sunstroke.

Symptomatology and Pathology. — In addition to the general disturbance of health which occurs in all who are more or less affected by heat — such as restlessness, irritability, sleeplessness — the morbid conditions which are to be attributed to the effects of a high temperature are: —

I. A. Syncope from exhaustion, caused either by the direct rays of the sun or a heated atmosphere in the shade; especially when the physical or mental powers are depressed: engine-room men in steamers in hot climates; men marching, or on parade, if oppressed with clothes or accoutrements, or weakened by previous illness, or by dissipation; labourers or artificers; men in hay-fields in England, or in heated rooms

and factories, in barracks, hospitals, tents, or ships, may suffer in this way. The condition is one of depression; the skin is cold and pale, and the pulse feeble. Death may occur from failure of the heart, but recovery is usual.

B. The exhaustion above described having passed away may be succeeded by fever, which may assume an ardent type [*vide* section on Indian fevers (thermic fever)]. The fever may, after a certain duration, defervesce; or it may result in changes, the consequence of damage done by the heat to the cerebro-spinal centres. Thus a variety of morbid conditions may ensue, depending upon the parts affected. Such cases are often very prolonged, and the only hope of recovery lies in removal to a colder climate.

When death occurs rapidly at the time of the exposure it may be due to sudden cardiac failure, as shown in the experiments of Claude Bernard and Brunton (8) upon animals exposed to great heat. When it occurs suddenly, during great exhaustion or muscular action with fatigue, it may be due to coagulation of the cardiac myosin, which Dr. Wood of Philadelphia has shown to be likely to occur during any great muscular exertion at a much lower temperature than usually determines it when there is no great muscular exertion. For example, men fighting in a very high temperature may fall dead suddenly; but probably coagulation of myosin is most frequently a post-mortem change.

II. The gravest and perhaps most fatal forms of sunstroke occur as a consequence of the general heating of the whole body, blood and tissues, which may happen either from prolonged exposure to the sun's rays in a heated atmosphere, to a heated atmosphere in the shade (occurring, as it does, by night as well as by day), or to an abnormal thermotaxic state due to vaso-motor or other heat-regulating disturbance.

In the first case the effect of the high temperature tells upon the brain, which becomes heated to a degree incompatible with due performance of its functions: this may result in acute cerebral symptoms, and sometimes in phrenitis, rapidly passing into a state of asphyxia, if the respiratory centres are involved: more frequently, perhaps, the whole body becomes overheated, the temperature rising to 106°, 108°, or 110°, which, if not rapidly counteracted, proves destructive to life by asphyxia or sudden cardiac failure, or even by cerebral hæmorrhage or meningitis.

In heat exhaustion the primary symptoms are those of depression. The person becomes faint, pallid, with a pale, cold, and moist skin and feeble pulse, not unfrequently attended with sickness. The soldier on parade staggers and falls over in a faint; so with the orator when speaking, or the artisan in pursuing his calling. This may take place either in the sun or in the shade. The condition is one of syncope, and may approach collapse; if reaction be not soon established death may result from cardiac failure, but this is rare. Recovery is generally complete, but when the state has occurred from direct application of intense solar heat and glare, the mischief is not always confined to the transient shock or impression; secondary effects, such as vertigo, muscular tremors,

and temporary loss of power may result; or a reaction may be followed by fever, or by symptoms indicating lesions of the centres or cerebral excitement, and this may end in mania.

In insolation proper the premonitory symptoms may appear some hours or even days before the dangerous symptoms set in, as the result of continued exposure to a high temperature; although they may occur also in a much shorter period, as when men are exposed in marching or in other occupations to a very high degree of solar heat, in which case some would no doubt be affected by heat exhaustion, whilst others would pass into a state of hyperpyrexia as before described. These are generally malaise, restlessness, insomnia, apprehension of impending evil, precordial anxiety; hurried, gasping, shallow breathing; a feeling of constriction round the thorax; vertigo; headache, often severe; nausea, or even vomiting, anorexia, great thirst, frequent micturition, and fervent heat of the skin. As one or more of these symptoms become aggravated the temperature rises to 104°, 106°, or even 110°. Dyspnœa and restlessness increase; the head, face, neck, and skin of the body generally become red, or livid, sometimes dry, sometimes moist; the pulse full and labouring, carotid pulsation very perceptible, pupils contracted, but dilating widely before death. Unconsciousness passes into complete coma, stertor, and epileptiform convulsions; finally, relaxation of the sphincters and suppression of urine precede death.

These symptoms all indicate a profoundly disturbed state of the cerebro-spinal centres and a disordered condition of the blood. The hyperpyrexia is incompatible with a due performance of their functions, and death will rapidly result unless prompt aid be given; indeed, it frequently does so despite all treatment. The fatal result is due to asphyxia and cardiac failure. There may be — though perhaps rarely — meningitis or cerebral hæmorrhage or effusion, the disordered state of the blood not unfrequently manifesting itself by petechial patches on the body.

The earlier stages of this condition are those of so-called thermic fever. A very high temperature may be maintained for several days, and finally defervescence takes place without evidences of any structural lesion; but unless active measures be used and the temperature rapidly reduced, unless, that is, the causes which produce the hyperpyrexia be mitigated or removed, the case is apt to pass on into the grave state, and to terminate fatally by paralysis of the respiratory centres, and in some instances, though rarely, by cerebral hæmorrhage. From the graver forms some recover, but many are permanently injured, and become invalids for life; life indeed is not unfrequently shortened by obscure cerebral or meningeal changes which affect the sufferer in varying degrees of form and intensity, such as epilepsy, irritability, impaired memory, cephalalgia, blindness, or deafness, partial or complete paralysis, dementia or even mania. In those who have apparently recovered intolerance of the sun's rays or even of the heat of temperate climates may remain; or such cases may after a long time end in dementia, or epilepsy, or

both; or in chronic meningitis with thickening of the calvaria; frequent or intense headache, general functional derangement and disordered innervation being persistent.

Morbid Anatomy. — When death has occurred in the syncopal form there is not any very obvious morbid change. The brain with its membranes and the lungs are sometimes but not always congested. The venous trunks in the abdomen and also the right cavities of the heart may be full of blood, which is imperfectly coagulated and deficient in oxygen. The abdominal viscera are congested; lividity of the body and decomposition come on rapidly after and even before death.

In death from thermic fever and insolation the heart is sometimes found firmly contracted — it may be from coagulation of the myosin — and the venous system generally is engorged. The blood is dark, grumous, fluid, and acid in reaction; the blood globules are crenated and do not rapidly form into rouleaux. The body for some time after death retains a high temperature. In early autopsies, necessary in hot climates, the body and viscera when opened feel pungently warm, dark blood drips freely from the incision, rigor mortis comes on rapidly. The brain and membranes are often congested. There may be some cerebral hæmorrhage, effusion of serum into the substance or cavities, or incipient symptoms of meningitis.

A precise degree of blood temperature incompatible with life cannot be defined, but the danger becomes very imminent at or above 108° or 109° F.

Prophylaxis. — Prevention is the great desideratum. The clothing should be very light, and woollen material should always be worn next the skin, as cotton or linen wet with perspiration is very injurious. The head and spine should be protected from the direct rays of the sun out of doors by a pith hat and a cotton pad let into the coat over the back of the neck and spine, and by a good white umbrella lined with green. The clothing should be loose, not constricting the neck or any part of the body. Indoors the temperature should be reduced by the use of thermantidotes, punkahs, or other artificial means of cooling; free ventilation should be insisted on, and a sufficient amount of cubic space — not less than 1000 to 1200 cubic feet per head — in sleeping rooms, barracks, and so on. During the hot, still nights — a most dangerous time — the foregoing precautions are especially necessary.

Overfatigue, excitement or depression should be alike avoided, though a moderate degree of exercise, physical and mental, is desirable during the cooler hours of the day. A short sleep during the course of the day is also to be encouraged.

For soldiers all drills not absolutely necessary should be avoided. If they must march during the hot weather it should be in the early hours of the morning. Frequent halts should be allowed, and coffee and a biscuit given out. Plenty of water should be carried and be readily available. The dress should be light and loose, and all con-

striction carefully avoided. The halts should be in the most sheltered places that can be found, with plenty of fresh air — such as open topes of trees. The accoutrements should be as light as possible, so as to spare fatigue and exhaustion. Men falling out should be attended to immediately by the medical officer. The marches and drills in the great heat should be as short as the exigencies of the service will permit.

Moderation of diet is especially to be enjoined. Very little animal food should be taken; the food, whilst sufficiently nutritious, should be light and unstimulating. Iced water should be drunk freely and frequently, and the greatest moderation in the use of stimulants should be observed. Excesses in eating, drinking or smoking are especially to be deprecated. The cold bath may be freely used. In short, regulation and moderation in all things, and careful attention to the state of the bowels, which should never be allowed to be confined, are essential. No one is more likely to suffer from the ill effects of heat than he who has undergone mental or physical exhaustion, or has suffered from intemperance in food or alcoholic drinks. Healthy persons who lead regular lives and observe such precautions will tolerate a degree of heat which would hardly be deemed credible.

Treatment. — In simple heat exhaustion, remove the patient to a cool place in the shade or into the open air, according to circumstances. Remove all oppressive or tight clothing. Dash cold water on the head and chest so as to rouse but not depress. If necessary, give a stimulant and apply ammonia to the nostrils. If depression continue, administer stimulants and restoratives; let the patient avoid exertion or exposure to heat as much as possible. In the steamers in the Red Sea and Indian Ocean stokers, usually Africans, are sometimes brought up from the furnaces unconscious from heat exhaustion, but are generally quickly restored by the fresh air, by dashing cold water on their bodies, or by giving a little stimulant.

If a man be struck down by the beating of the hot sun on his head, apply the cold douche freely to the head; if there be rise of temperature, apply ice to the head, but not for too long a time. The object is twofold, to rouse by reflex action and to reduce temperature.

At the capture of Rangoon in 1852, numbers of men under my observation were struck down by the sun, some simply from heat exhaustion. They were clad in the thick red coats worn in India in those days. In others, apparently, the exhaustion was combined with the direct effects of the sun upon the head and spine. They were all douched with cold water and placed in the shade in the Field Hospital. All but two recovered; these two were bled on the field where they fell, and never regained consciousness. By recovery is meant a favourable reaction at the time; in some there were consecutive symptoms of fever and cerebral disturbance; they were sent away to a Depôt hospital, and if their history could be traced, it would probably be found that in some of them complete recovery never took place. Exposure to the sun's rays should be carefully guarded against, and unless recovery

be rapid and complete, a colder climate should be sought, where the same precautions must be continued.

In thermic fever or insolation the object is to reduce the temperature, before more serious or fatal consequences appear. For this purpose quinine in doses of 5 grains, or even more up to 10 grains of hydrochlorate or sulphate, may be given in solution by the mouth, every three hours; or the equivalent in the form of a hypodermic injection [*vide* article on "Indian Fevers"], may be given and continued until an impression is produced. Morphia has also been suggested, but this practice seems questionable. Bleeding should not be resorted to except in special cases. In asphyxia, where the right heart is overloaded, it may be expedient in the choice of evils. As a general rule it has been abandoned, for though it may have appeared at first to produce a favourable impression, subsequent results have not justified it as a general practice. No absolute canon of procedure can be laid down with reference to bleeding in this disease; each case must be dealt with on its own merits. All that can be said here is that it is not desirable as a general rule. Should the quinine not be effective in reducing the temperature, antipyrin, phenacetin, antifebrin, aconite, or acetate of ammonia may be tried.

The cold bath, cold affusions, and application of ice to the head — which should be shaved — and to the body, should also be resorted to, care being taken not to prolong the cooling until too great depression be produced — that is, not below 100° F. The bowels should be relieved by calomel, colocynth and saline purgatives, and by enemata; care being taken that sufficient daily action be maintained. In the epileptiform convulsions which sometimes occur the cautious inhalation of chloroform may be resorted to. I have seen good results from its use. Blisters are sometimes applied to the nape of the neck, but it seems doubtful whether, in the early stages at any rate, they can be of much use, if any. Light and unstimulating diet should be given in small quantities at tolerably frequent intervals. This antipyretic treatment must be continued as long as a high temperature lasts, to obviate the imminent risk of death or of tissue changes which may be permanently injurious. As the case proceeds, if symptoms of cerebral or meningeal mischief supervene, iodide and bromide of potassium and counter-irritation may be of service.

It is essential that perfect rest of mind and body should be maintained. When insomnia is distressing hypnotics may be useful; they must be given with great caution, and without opium if it can be avoided. Restriction should be imposed upon the use of alcoholic stimulants. The amount, if any, that may be given must depend upon the previous habits as well as the present condition of the patient. Here, again, the physician must be guided by the special indications of the case before him. Precautions should be continued, not only when recovery has set in, but even for some time after it is apparently complete; for certain indications of latent chronic mischief will probably remain, such as loss of memory, irritability, headache, inability to concentrate the

thoughts, intolerance of heat, or of the slightest exposure to the sun or even of the temperature of an overheated room. Not until these have completely disappeared can a return to India or any other hot climate be permitted with any propriety or prospect of future health. I repeat that frequently, indeed, a patient can never return to a hot climate at all.

It seems hardly necessary to say that cases of this kind should be removed from a hot climate to a colder one as soon as travelling can safely be permitted, and that the sufferers should be carefully watched on their way home. Neglect of this precaution has resulted in self-destruction during the mental aberration that sometimes follows.

The sequelæ of sunstroke occasionally assume a serious character, and are the cause of permanent disability to the patient and a source of much anxiety to his friends. The slighter forms of meningitis and of cerebral mischief not unfrequently pass away after protracted residence in a temperate climate, but they are also not unfrequently permanent, and endanger or shorten life, causing such physical or mental disability as epilepsy, partial paralysis, mania, chronic dementia, impaired memory, and inability for mental concentration — sad examples of the evil effects of a tropical or hot climate.

Treatment will depend upon the nature and extent of such mischief. These vary so much as to render it impossible to give more definite directions here, and the reader is referred to the special chapters of this System on Cerebro-spinal and Mental Diseases.

I am indebted to Brigade-Surgeon Lieutenant-Colonel Hooper, Civil Surgeon of Lucknow, for the following cases of insolation, which illustrate the hyperpyrexial symptoms, and the treatment by the application of cold, quinine, and other remedies.

In all these cases but one recovery seems to have followed; but the subsequent history of some of them, could it be ascertained, would probably show that such sequelæ as have been described in the text ensued.

No. 1. — Case of Insolation; Death on Third Day

A private soldier, European, æt. 22, was admitted into the hospital, Lucknow, on 4th June 1892; unconscious, breathing stertorous, temp. 106°, pupils contracted, reflexes abolished. Treated with douching, sponging with iced water, enemata, sinapisms, and injections of strychnine. Temp. fell to 97·8° F., but consciousness was not recovered. Pulse feeble, respirations very shallow and quick, limbs very rigid. Pulse gradually failed, respiration quick and shallow, conjunctivæ injected, cornea ulcerated; temp. went up again, and had reached 105° F. on the morning of the 6th. He died on morning of 7th.

Post-mortem. — Sinuses of dura mater distended. No excess of fluid in arachnoid.

Brain congested, with marked puncta cruenta. Ventricles filled with serum.

Lungs crepitant, and not much congested.
Liver, spleen, and *kidneys* all greatly congested.

No. 2. — Case of Insolation; Recovery

Private soldier, European, æt. 34, admitted into hospital, Lucknow, on 22nd June 1892. Feeling sick and dizzy all day. In the evening temp. rose to 109°. Cold douche applied and turpentine enemata given. Temp. fell to 99·8° F.; continued a little raised for a few days. Thirty grains of quinine given daily. Discharged on 10th July.

No. 3. — Case of Insolation; Recovery

A private soldier, European, æt. 22, was brought into hospital, Lucknow, on 19th May 1894. He was unconscious, skin very dry and hot, temp. 110° F. in the axilla, eyes fixed and staring, conjunctivæ congested and insensitive, pupils dilated, breathing stertorous, and pulse almost imperceptible. He was put into a cold bath for about ten minutes, then into a wet pack; ice was applied to the head and back of the neck, and he was fanned. Cold water was injected into the rectum, and a large quantity of fæces came away. Brandy and ether were injected subcutaneously, and a small enema of brandy and water was given, but the latter was soon rejected. After a time the temperature came down to 102°, and the breathing became easier. Convulsions were painful and frequent; chloroform was used, and dry cupping along the spine. The pulse became stronger after about six hours, the pupils slightly sensitive to touch, and congestion of conjunctivæ diminished; but convulsions still occurred if he were touched or a hand passed in front of him. Two injections of morphia, $\frac{1}{6}$ gr. in each, were administered. The patient did not recover consciousness for over twenty-four hours, and then only when roused. There was emphysema of the connective tissue of the left side of the face and neck, extending as far as the clavicle and over the deltoid muscle, and also under the axilla. The voice was thick; the eyes were very sensitive to light, and the patient was kept for some time in a darkened room. Cold water continued to be applied to the head, and iodide and bromide of potassium administered. On the fourth day after admission the temperature became normal; it rose slightly subsequently, but recovery was uninterrupted, and the patient was discharged on 20th June. He was sent to a hill depôt on 10th July.

No. 4. — Case of Simple Insolation; Subsequent Cerebral Symptoms; Recovery

An officer, æt. 34, was admitted into hospital on 27th March 1894 with severe pain in the head, from which he had been suffering for some days. On 17th March, after riding in the sun all day, he was seized with pain in back and aching in limbs. He went out shooting the next day, and pain in the head with fever came on the same evening.

On admission; temp., abdomen, liver, and spleen were normal. On the evening of 28th, while in bed, he had a prolonged attack of syncope, nausea, cold sweats, weak and frequent pulse, pallor, vertigo, hurried respiration. This passed off on the administration of brandy. The pain in the head ceased, but dizziness and sickness came on when he tried to raise it. Potas. iodide and sp. ammon. aromat. administered. On 1st and 4th April temp. rose to 101° and 100° as result of attempt to sit up in bed; vertigo also increased, with buzzing in ears. The iodide of potassium was discontinued, 10 grs. of quinine administered daily, $\frac{1}{2}$ gr. of calomel morning and evening. After this date the improvement continued, the vertigo diminished, but was induced by any sudden head movement. Was discharged on 25th April for three months' leave. For many months afterwards vertigo came on with any sudden movement of the head, and headache was induced by the slightest exposure to the sun.

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PART II.—THE INFECTIONS[1]

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[1] The Infectious Diseases will be described in the above order, which was drawn up for me by Dr. Kanthack, and kindly revised in parts by Dr. Manson. (*The term Bacteriology includes the study of all morbiferous micro-organisms.*) —Ed.

THE GENERAL PATHOLOGY OF INFECTION

I. Bacterial Forms

Bacteriology deals with the lowest forms of vegetable organisms, and so far as it concerns itself with the biological phenomena of these lowly beings it is a part of botany. But since bacteria are found in many diseased processes, bacteriology necessarily also forms a part of pathology, that is to say of medicine. Our knowledge of disease cannot then be complete without a fair grasp of the part played by the micro-organisms. Many symptoms and obscure changes are thus readily explained; the treatment of maladies, and the rules of prevention — the highest form of therapeutics — are often laid down or indicated by the bacteriological pathologist. Because so much new light has been thrown on diagnosis and prognosis in disease, because some of our recent therapeutic triumphs have been achieved by bacteriology, a System of Medicine would fail to be complete if it did not offer some information on the elements of this the youngest branch of pathology. While undertaking this share of the work, I feel not only the great responsibility, but also the difficulties which accompany it, and further realise that the physician cannot often be a bacteriological specialist; he desires, however, to learn the bearing of bacteriology on the clinical phenomena of disease and its application to practice. In the lines that follow, therefore, I shall endeavour to give a general view of the facts and opinions which the study of bacteria has either disclosed or indicated, in so far as they directly concern the clinical physician; whether for the purposes of diagnosis and prognosis, or for those of treatment and prevention.

Obviously we must begin with a short account of the general morphology and biology of bacteria, that is, with so much of it as is necessary to demonstrate the influence of bacterial life and activity in disease.

Morphology of Micro-Organisms. — The vegetable micro-organisms, so far as we have to deal with them, have been classified by Nägeli under three headings, namely, I. Hyphomycetes or Moulds, II. Blastomycetes or Sprouting Fungi, III. Schizomycetes or Cleft Fungi. Others have singled out the schizomycetes as mycetes or microbes, but, rightly or wrongly, these terms are commonly applied to all the three groups of micro-organisms in a generic sense; and when no harm is done thereby it is well to bow to custom.

I. Moulds or Hyphomycetes. — These organisms are characterised by a mycelium or interlacing network of filaments which constitutes the fungus itself. From this mycelial network there extend other filaments (hyphæ) which bear the fruit-bearing organs and spores. The formation of these spores varies in the different forms, for (*a*) in some cases the terminal cell of the hypha undergoes transverse division (conidia), or (*b*) in others it enlarges, forming a receptacle enclosing the spores

(sporangium or ascus), or (*c*) two hyphæ fuse and at the point of union the spores develop (oospora). Fuller descriptions will be found in works on Botany.

The following moulds are the more important among those found either in disease or in ordinary human surroundings: —1. Penicillium glaucum (not pathogenetic). 2. Oidium lactis, found almost invariably in sour milk (not pathogenetic, though formerly supposed to be the cause of thrush). 3. Trichophyton tonsurans, found in ringworm. 4. Achorion Schönlein, found in favus. 5. Microsporon furfur, found in pityriasis versicolor. 6. Monilia candida, said to be the cause of thrush. 7. Mucor: various forms of this widely-distributed genus have occasionally been obtained from man, especially from the external auditory meatus. 8. Aspergillus: two varieties. The A. niger and A. fumigatus have occasionally been found in man, for example, in so-called pneumomycosis, in purulent conditions of the middle ear and of the antrum maxillare. 9. Actinomyces, pathogenetic for man and cattle. Its exact botanical position is not yet settled; some classify it with cladothrix, others with streptothrix. [This fungus will be fully considered in the article on "Actinomycosis."] 10. Streptothrix: various forms of pathogenetic streptotriches have been described. These organisms resemble the actinomyces closely.

We are still comparatively ignorant of the physiological properties of these mould-fungi. Many of them certainly exert a fermentative action: thus Penicillium glaucum is able to convert cane-sugar into other sugars; some aspergilli contain a diastatic ferment which converts starch into dextrose and maltose; some species of mucor are able to act as true alcoholic ferments, and Monilia candida will even ferment cane-sugar as such without previously inverting it. The various lesions produced by some of the above-mentioned fungi will be described under their proper headings.

II. Blastomycetes or Sprouting-Fungi. — These organisms are fairly large round or ovoid cells which, generally speaking, multiply by budding. As a rule they appear as separate cells unconnected by any mycelium, though among the budding-fungi there are some which under certain conditions will form a mycelium. Again, although they mostly multiply by means of budding, there are some which possess the property of forming spores in the substance of the cell (endogenous spore-formation).

Three groups may be distinguished:—1. Saccharomyces: budding-fungi; mostly without a mycelium; the cells are sometimes nucleated, occasionally form endogenous spores, and generally are capable of inducing alcoholic fermentation. 2. Torula: multiply by budding, form a mycelium only exceptionally, never form spores; some have a pronounced fermentative activity. 3. Mycoderma: variously shaped cells, containing refractive particles; they form a film on the surface of the fluid on which they grow, and possess either no fermentative activity, or but little.

The pathological importance of these forms is not great, though pathogenetic torulæ have recently been described. However, as they are so widely distributed that some varieties are constantly found in

the human excretions, a slight acquaintance with them is desirable. Some writers consider the thrush fungus to be a variety of mycoderma.

III. Schizomycetes or Fission-Fungi. — Most pathogenetic organisms, or at any rate those which are best known to us, belong to this group of minute, unicellular vegetable organisms. They owe their generic name to the fact that they divide or multiply by fission. The schizomycetes, so far as the pathologist knows them, are small, minute cells, visible only when examined under the highest powers of the microscope (oil-immersions) with the best possible illumination (Abbé's substage-condenser); they are devoid of a nucleus, at any rate a true nucleus has not been demonstrated. When dead and dried they have an affinity for basic or nuclear dyes, such as methylene blue, gentian and methyl violet, and fuchsine. Living bacteria refuse to take up the dye in a satisfactory manner; but when allowed to dry on a cover-glass and fixed by heat, they are stained readily, unless they have been fixed in a state of degeneration or involution. They refuse acid dyes, such as eosin, acid fuchsin or picric acid. Although they may all be stained with basic anilin dyes, they vary greatly in the readiness with which they imbibe the stain. Thus tubercle bacilli are stained with difficulty, and only with the assistance of mordants; leprosy and glanders bacilli likewise require time and patience, if not skill. On the other hand sarcinæ and pyococci are easily overstained. It is impossible to lay down general rules as to the time of exposure to the dye, or as to the particular dye, required for the various organisms. Experience is the only guide.

The schizomycetes in ordinary medical language are called bacteria; in fact these two names have become almost synonymous. From the botanist's point of view this is undoubtedly incorrect; the convenient confusion of terms is, however, sanctioned by usage, and we may safely accept "bacteria" as the generic term interchangeable with schizomycetes. Bacteria are generally classified according to their morphological distinctions — that is, their shapes and forms — as 1. Cocci; 2. Bacilli; and 3. Spirilla. This classification is not a natural one; but so long as we are unacquainted with the exact relation of these forms to each other, it is less perplexing to use a provisional classification which is both practicable and easy.

We shall now consider these three subdivisions in detail: — 1. The *Cocci* or *Micrococci* are minute spheroidal or oval cells, and, when growing in artificial media or in the animal body, they always remain cocci; their spheroidal form is constant. The cocci are again subdivided according to their arrangement or grouping. Thus we may have (*a*) paired cocci, that is, cocci arranged in twos, the so-called *Diplococci*. These are often surrounded by a distinct capsule, which may be stained by appropriate methods. As examples may be mentioned the capsular pneumococci and the non-capsular gonococci. (*b*) The cocci may be arranged in chains, when they are called *Streptococci*. These chains may be either short or long. The shortest streptococci consist of two component members. Thus we find that the pneumococcus, which in the animal body is generally an encap-

suled diplococcus, occasionally appears as an encapsuled streptococcus of four or five or six component elements; and on artificial cultivation, especially in liquid media, it frequently develops as an ordinary non-capsular streptococcus. The encapsuled diplococcus is therefore the most primitive and simplest form of streptococcus. (*c*) The *Tetracocci* are grouped in fours, often enclosed in a capsule, though on artificial cultivation the capsule is frequently lost. (*d*) The *Sarcinæ* appear in packets of eight or more cocci. (*e*) If the cocci are arranged in irregular clusters, or in heaps of no particular shape and devoid of symmetry, we name them *Staphylococci*. Tetracocci and sarcinæ on artificial cultivation not infrequently appear as staphylococci; and sarcinæ again under such conditions often appear as non-capsular tetracocci or as diplococci; so that the tetracocci or sarcinæ, or the non-capsular diplococci, may be regarded as the simplest forms of staphylococci. We see then that there is no constancy of arrangement here, though the constancy of individual form is always preserved; that is, diplococci may develop on the one hand into streptococci, on the other hand into staphylococci; tetracocci readily transform themselves into staphylococci, but in every case, streptococci remain always streptococci and never become staphylococci; and conversely staphylococci are never changed into streptococci. The staphylococci clusters are often held together by a tough mucous material; such clusters are termed *zooglœa*.

2. The *Bacilli* are rod-like structures, that is, they have a long diameter often considerably longer than the transverse. These rod-like organisms may be very short and plumb, or they may be long, thin and graceful; they may have pointed or blunted ends; they may be arranged in pairs, in short and long chains, or in filaments. When fusiform or spindle-shaped in appearance they are often called *clostridia*.

Dr. Klein and others have shown that some bacilli — for example, the tubercle or diphtheria bacilli — have a tendency to form true mycelial threads, which would suggest that these organisms possess a fungus ancestry; others, like the anthrax bacillus, assume a yeast-like appearance on artificial cultivation. On the other hand, the actinomyces when grown in the laboratory generally passes through a bacillary phase before it obtains its fully developed mycelial structure. These facts are of great importance, because they remind us of our imperfect knowledge of bacterial morphology. This variability of form, termed polymorphism or pleomorphism, will be discussed later.

3. The *Spirilla* include all the curved or spiral forms. At one time a distinction was made between the spirilla and the vibrios, which are slightly twisted bacteria, or curved bacilli. The latter were also called comma bacilli, as for example the organisms of Asiatic cholera. Now we know that the vibrios and comma bacilli easily grow into true spirilla, and that we are here dealing with a good example of pleomorphism. We shall therefore speak of "spirilla," and more properly call the comma bacillus or vibrio of cholera the spirillum of Asiatic cholera. It appears that under certain conditions the vibrios or spirilla may lose

their curved appearance, and become transformed into straight bacillary structures.

The cell substance of these various bacteria is generally colourless, refractive and homogeneous; but occasionally it is granular or vacuolated. Many bacteria are enclosed by a distinct cell membrane; it is doubtful, however, whether they all possess an enclosing sheath.

We must now consider a few special morphological features of the bacteria, features either recognised as specific characters, or of biological importance. These are — 1. Spore-formation; 2. Flagella or cilia; 3. Involution forms; 4. Pleomorphism and variability.

1. *Spores.* — Most micro-organisms multiply by binary fission; many, however, are capable also of a higher or more specialised form of proliferation; namely, by means of spores.

Spore-formation has been observed hitherto in bacilli only; micrococci never possess true spores. When fully developed, the spores appear as well-defined, sharply-contoured, highly-refractive bodies, round or oval in shape. They are either central or terminal; that is, the spore may occupy the middle or one or other extremity of the bacillus. In the latter case the spore-bearing organisms have the shape of a drumstick: the tetanus bacillus and some water and intestinal bacilli are the best examples of this type. When the spores are centrally situated the bacillus itself may become swollen and spindle-shaped (clostridium), as in the case of the Bacillus acidi butyrici; or the spore may develop without producing any morphological change in the bacillus. Occasionally before or during the spore-formation the bacilli grow out into long threads or filaments, in which a beaded series of spores appears, as in the case of the Bacillus anthracis; or the bacilli themselves increase in length, as in the case of the tetanus bacillus. Spores which are developed in the substance of the bacillus, whether central or terminal, are described as *endogenous spores* or *endospores*. Each bacillus contains only one spore, which is eventually freed by leaving its parent, or by the death of the latter. Under favourable conditions these spores germinate and are again developed into bacilli. They are highly resistant to external influences, — such as drying, heating, disinfecting, etc., — more or less serious disturbances which destroy the bacilli themselves, being easily withstood by their spores. These resisting powers, however, vary greatly; some spores, like those of the tetanus bacillus, remain unaffected after being heated for an hour at 80° C.

Spores are formed under certain conditions only; there must always be the optimum of air, warmth and nourishment—conditions which vary, of course, for each organism. Thus the anthrax bacillus requires a sufficient amount of air (or oxygen) and of warmth, and it refuses to form spores in the animal body, or at a temperature of 42°–45° C., or if certain substances, such as carbolic acid or alcohol, be added to the broth in which it is grown. By continued cultivation in carbolised broth, or at 42° C., this bacillus may permanently lose its property of forming spores, and become "*asporogenous*"; although the morphological appearances

are not otherwise modified. Although strongly resistant to most external influences, the spores of many bacilli — for example, of bacillus anthracis — are killed by a comparatively short exposure to direct sunlight in the presence of air.

In studying the ætiology of infective diseases it is important to investigate the power of spore-formation possessed by any particular bacillus, for this is to some extent a measure of the resistance on the part of the infective organism, and therefore of the risk of infection or contagion. Asporogenous organisms, speaking generally, die sooner, or are more easily destroyed by antiseptics and disinfectants, and their distribution is often more narrowly limited. To this point we shall return.

Besides endogenous spores, another form of spore, — the so-called *arthrospore* — has been described, especially by De Bary and Hüppe; their existence is however, doubtful. Arthrospores are supposed to be members of a chain or group of micro-organisms which acquire a greater vitality or power of resistance, and thus become the starting-point of new life. They may be characterised by increased size and refraction. It is said that streptococci may persist, or may be perpetuated by arthrogenous spore-formation. Certainly on examining chains of such cocci we often find larger and more striking individuals — two or three times as large as other members of the chain — but it is doubtful whether these peculiar forms are really spores. They stain readily with ordinary aniline dyes, while endospores stain with difficulty, and only by means of special and elaborate methods: moreover, they seem to be no more resistant to external influences than the ordinary cocci. The whole subject of arthrospores is still in obscurity.

2. *Flagella or Cilia.* — It has been known for a long time that many micro-organisms possess the power of spontaneous movement. When examined under the microscope in a drop of fluid — in a hanging drop — they are seen to move across the field, sometimes floating away quietly and slowly, sometimes darting across quickly, sometimes propelling themselves with a screw-like action. Bacilli and spirilla or vibrios especially are motile, though some micrococci also share this property. Löffler has shown by special and difficult staining methods (which since have been made much easier), that such organisms generally possess flagella or cilia by means of which they propel themselves. Some bacilli have only one or two such flagella; others — as, for example, the typhoid bacillus — are completely surrounded by them: some, again, have a single flagellum at one or other end, or at both ends; others a bundle of terminal flagella. The vibrios, as a rule, have one, two, or three cilia at one extremity. The rapidity of movement seems, as a rule but by no means always, to vary with the number of flagella. The ciliary processes also vary considerably in length, thickness and shape, and appear to spring from a sheath around the bacterial cell; as a rule they are very much longer than the organisms bearing them, and are spirally twisted. It appears that some organisms, although incapable of spontaneous movement, nevertheless possess cilia, for example the bacillus anthracis. It

would seem that for a given species of bacillus or vibrio the number of flagella is constant or varies within narrow limits, so that these have become important morphological factors, and are often of great use in distinguishing between allied or similar forms. Thus the bacterium coli commune closely resembles the typhoid bacillus, but it possesses few flagella, varying from one to six, or ten, while the Eberth-Gaffky bacillus is completely surrounded by them. At the same time, it must be remembered that the flagella are extremely brittle, and are often missing in greater or less numbers.

3. *Involution Forms.* — Under certain conditions micro-organisms, especially the bacilli or the vibrios, become altered in shape, losing their ordinary form, or becoming even quite unrecognisable, it may be through age, exhaustion of the nutrient medium, or other harmful influences. Thus the vibrio of Asiatic cholera, when kept for some time, may become bacillary or coccoid in shape; bacilli, again, may become beaded or varicose, shorter or longer. On transferring such aberrant forms to a fresh soil, or on placing them under more favourable conditions, unless they have degenerated or have aged past all recovery, they assume their original shape and structure. Abnormal or unusual forms, in healthy, young, and vigorous growths, must not be confounded with involution forms. Thus, diphtheria bacilli, grown on the surface of blood serum or agar-agar, often become elongated, clubbed, or branched; tubercle bacilli also show a tendency to elongation and branching or clubbing; anthrax bacilli may grow as yeast forms. Here we have either a pleomorphism (or polymorphism), or a reversion to an ancestral type which is best seen in young colonies; but involution invariably implies degeneration.

4. *Pleomorphism and Variability of Form.* — Koch originally upheld the doctrine of the constancy of form, "die Konstanz der Form." Broadly speaking this is true enough; most pathogenetic organisms adhere to one type or form; but many micro-organisms show a great tendency towards variation. Thus vibrios often become spirilla; the ray fungus passes through a coccoid and bacillary stage; the diphtheria bacillus may either be long, short, straight, or clubbed. True, a streptococcus will never become a staphylococcus or a bacillus; but, as a streptococcus, it will vary, growing occasionally in short chains, occasionally in long chains; sometimes in the shape of fine small dots, at other times as larger and plumper cocci. This diversity of shape among organisms of the same species is called pleomorphism or polymorphism, which terms simply imply individual differences. Thus if we were to cultivate diphtheria bacilli from a single bacillus sown in broth, we should find the descendants very variable in shape; some are small, others larger, some straight, others clubbed or branched: or starting from a single vibrio, we should find that some of its descendants are spirillar, others S-shaped, but most of them true vibrios. Pleomorphism must be carefully distinguished from variability: the former is a character belonging to a species, and is transmitted from generation to generation; variation of individuals depends on environment, some species, under the influence

of adaptation, being more easily changed than others, whether temporarily or permanently, so that new varieties or even new species may be produced. Upon what pleomorphism depends we do not at present understand: in some cases, apparently — as in those of the diphtheria and tubercle bacilli — it is assumed by Klein and others to be based on the ancestral history of the organism. We must carefully distinguish, however, between a true pleomorphism and an accidental contamination of a culture with extraneous organisms — a confusion of two very different things which, especially in the earlier days of bacteriology, led to many errors.

Variation may lead to change of form, or to change of function; the latter we shall consider subsequently. Degeneration and involution are no more variation than are disease and old age in animals. In most cases change of environments — that is, generally change of soil or temperature — produces merely temporary variations. Thus typhoid bacilli in ordinary broth will appear in one form, in carbolised beef-broth in a widely different one: so long as they are grown in these media they will retain these respective forms; but if transferred from carbolised to ordinary broth there is an almost immediate return to the ordinary shape. Similarly the Bacillus pyocyaneus in different media may be cultivated as a small bacillus, as a long rod, as a filament, and even as a comma form; but a return to the ordinary media is always followed by a return to the recognised form. Similarly variations in mobility and in arrangements and numbers of flagella may be temporarily produced by change of environments.

It seems extremely difficult to produce permanent varieties of form, but it is possible: thus the bacillus prodigiosus may be changed from the small bacillary into a permanent long bacillary form; and the anthrax bacillus may be converted into an asporogenous species. An extremely good summary of the variability of bacteria, by Professor Adami, is to be found in the *Medical Chronicle* for September 1892.

We are comparatively ignorant of natural variations, and the greatest confusion exists between varieties and species. This is well seen in the case of the choleraic vibrios: numerous forms of these have been obtained from cholera stools, which by some writers are regarded as varieties, by others as species — the former are probably influenced by their opinion that cholera is caused by one specific organism only, the latter recognise in them different and distinct forms of the comma-shaped organism. Now in the case of these various choleraic vibrios, we find that continuous growth in identical media leads to no assimilation of characters; they become modified under such conditions, but when the limit of modification, due to adaptation, has been reached, the acquired characters remain stable, and continued exposure to like conditions does not give rise to any general assimilation of characters in the similarly cultivated organisms. This being so, it would seem that we are dealing with species rather than with varieties. The question is, however, beset with so many difficulties that we must for the present be content with

an arbitrary standard based, perhaps, on preconceived ideas. As Dr. D. D. Cunningham says, "If the vibrio of Finkler-Prior is a different species from Koch's comma bacillus, its distinctive characters must be of specific value; if this be so, then, as many so-called choleraic vibrios differ among each other no more, or even less, than do Finkler-Prior's and Koch's vibrios, we must consider the various choleraic vibrios as so many species." Consistency must be preserved in all matters of doubt, and, whatever our hypotheses, we cannot without more evidence regard like differences as specific in one case and non-specific in another.

II. Biological Requirements

All bacteria, being protoplasmic cells, require food for further development and propagation, which must consist both of nitrogenous and non-nitrogenous substances. To study the vital phenomena of bacteria, however incompletely or unsatisfactorily, we must cultivate or grow them. In the laboratory we can only place them in conditions which approximate, often very slightly indeed, to those pertaining to them in nature. In most cases the artificial cultivation of bacteria in test-tubes and incubators has no pretence to resemble natural growth; it is merely an experimental device by which we seek to unravel the mysteries of microbic life. We vary the soil as much as we can, we alter the surroundings, we imitate what we suppose to be the natural state; but as we can never reproduce this exactly, our conclusions can only be regarded as approximations to the truth. In bacteriology conclusions are too readily drawn on incomplete evidence, yet in this study especially rigorous and unimpeachable evidence is required.

There is no uniform or general nutrient medium suitable for every form of microbic life either in the laboratory or in nature. Some organisms thrive best in highly albuminous media; others on or in substances poor in albumin: some grow better on a solid stratum, others in a liquid medium. No general rules can be laid down; for practical laboratory purposes we find that soluble and diffusible albumins and proteids are the best nitrogenous, and sugar or glycerine the best non-nitrogenous media. Some bacteria refuse to grow on any mixture we may compound or concoct; they refuse even blood serum and the living animal body — as for instance the leprosy bacilli; others will only grow in the living tissues; others again on dead matter only. A suitable artificial nutrient medium for bacteria must contain a preponderance of water, certain quantities of carbonaceous and nitrogenous organic substances, and in addition potassium salts and phosphoric acid compounds. As already mentioned, nitrogen is best supplied by means of albuminous substances, notably peptones; though urea and ammonium salts are useful substitutes. Some organisms are capable of obtaining their nitrogen from nitrates, which they gradually reduce to nitrites and eventually to ammonia. The best sources of carbon we find in the various forms of sugar, in mannite and in glycerine.

We cannot discuss these matters fully in a work on medicine; further information must be sought in special treatises, or better still, it must be gained by patient laboratory observation.

Of importance in the selection of artificial media are (*a*) the concentration, (*b*) the reaction, (*c*) the temperature, (*d*) the presence or absence of free oxygen, (*e*) the light, and (*f*) the atmospheric pressure.

(*a*) *Concentration.* — Some organisms are capable of thriving in extremely dilute albuminous solutions; the vibrio of Asiatic cholera, for instance, can be separated best by means of cultivation in weak peptone solutions.

(*b*) *The reaction* of our artificial media is generally neutral or faintly alkaline. Most organisms are sensitive to an excess of alkali or to an excess of acid, but some develop best in decidedly acid media.

(*c*) *The temperature* most favourable to growth in a test-tube varies, within certain limits, with the particular species. As a general rule it may be stated that all pathogenetic organisms found in morbid lesions of warm-blooded animals prefer 38·5° C., that is blood heat: conversely those which under natural conditions produce disease in fish and other cold-blooded animals are frequently capable of growth only at lower temperatures. There are also, however, many non-pathogenetic bacteria which refuse to grow above 20° or 22° C., especially many water and air organisms; and again, as Dr. Macfadyen has recently shown, there is a class of microbes which refuse to grow at any temperature below 50° C.; such organisms are called "thermophile." Microbic life is impossible at very low or at very high degrees of temperature. Numerous organisms, however, have been found in the snow crystals of freezing chambers, and in ice and snow. Experience alone can tell us the optimum temperature for a given kind of micro-organism.

(*d*) Most micro-organisms require free *oxygen* for their growth and development; but there are some which cannot thrive in an atmosphere containing oxygen. The latter are called *anaerobes*, the former *aerobes*. Amongst the anaerobes we find some which, though preferably anaerobic, can yet exist in an atmosphere containing oxygen; these are the *facultative aerobes:* and again there are some aerobes which possess the faculty of growing in an atmosphere deprived of oxygen; these are the *facultative anaerobes*. We have thus the following groups: —

Aerobic germs: — (i.) *Obligatory aerobes*, which must be supplied with oxygen. (ii.) *Facultative anaerobes*, which preferably grow under aerobic conditions, but may also exist as anaerobes.

Anaerobic germs: — (i.) *Obligatory anaerobes*, which can grow only in an atmosphere free from oxygen. (ii.) *Facultative aerobes* or organisms which preferably are anaerobic, but which may grow also under aerobic conditions.

Among obligatory anaerobic germs we find the bacillus of malignant œdema, readily obtained from garden earth; the bacillus of tetanus, another inhabitant of the soil, and the bacillus of quarter-evil. These bacilli can produce their poisons or "toxins" only in media wherein

they are sheltered from free oxygen. The best known facultative anaerobes are the pyococci, the bacillus anthracis, the bacillus of typhoid fever, the bacterium coli commune, and the microbes of pneumonia and of Asiatic cholera. The commonest obligatory aerobe is the hay bacillus or the bacillus subtilis. It is, however, impossible to draw a hard and fast line between the facultative anaerobes and the facultative aerobes.

The following are the various methods in common use to obtain the suitable conditions for *anaerobiosis:* —

1. The oxygen may be removed by means of a solution of pyrogallic acid in caustic potash (Buchner's method). This is the best and easiest way of obtaining an atmosphere free from oxygen.

2. The organisms may be grown *in vacuo* by means of exhausting the tubes or flasks containing the inoculated nutrient medium.

3. The atmosphere may be replaced by an indifferent gas, preferably by hydrogen.

Whatever method be used, reducing substances may be added, at the same time, to the media in which the organisms are grown; such substances are glucose, formate and sulphindigotate of sodium.

Many pathogenetic organisms, though in the laboratory generally cultivated under aerobic conditions, in the animal body must grow as more or less strictly obligatory anaerobes. Thus in deep or closed abscesses oxygen is either absent or present only in minute traces. There can hardly be any doubt that the chemical activity of the pathogenetic bacteria must vary under such opposed conditions as aerobiosis and anaerobiosis. In the absence of oxygen facultative anaerobes will often display a most extraordinary fermentative action. We are still far too ignorant of the minute changes, chemical or physical, in the tissues to speculate with any degree of promise; but this much is certain that, even if we choose media most closely resembling the tissue substances, we cannot reason directly from changes in the test-tube to changes in the animal body, because the conditions of atmosphere and oxygen among others, are or may be extremely different.

(*e*) Recent researches have shown that many bacteria are injured by *sunlight;* and speaking generally, it is best to cultivate organisms in the dark. Prof. Marshall Ward, who has paid especial attention to this subject, has shown that the blue and violet rays of the spectrum are especially destructive to certain forms. Thus anthrax spores, which are extremely resistant to external influences, typhoid bacilli, and choleraic spirilla soon die when exposed to the rays of the sun; tubercle bacilli are either attenuated in their virulence or destroyed; and chromogenetic organisms lose their power of producing pigment, and in some instances are converted into colourless varieties. It has been shown that these effects are not due to the heat rays; they appear to be the result of oxidation; for in a vacuum, or in the depth of the nutrient medium, insolation is less effective or even powerless. Some observers think that ozone, formed by the action of the solar rays, acts as a strong germicide; others suggest that hydrogen peroxide is the destructive agent.

It is asserted by some observers that the quality of the nutrient medium is not altered by the light; that the action is a direct one, affecting the organisms in the medium: others, however, maintain that insolation may have a deleterious or unfavourable effect on the soil. Even diffuse sunlight has an inhibitory or noxious effect on the growth of certain forms of micro-organisms. It must not be imagined, however, that all organisms are injured alike by the solar rays; some grow well or even more vigorously in sunlight. It has been found that the solar rays are capable of destroying or rather of decolorising solutions of some of the bacterial pigments, for example, the green or blue pigment of the bacillus pyocyaneus dissolved in chloroform, or the red pigment of the bacillus prodigiosus extracted by ether or water. And here also it will be seen that the blue rays are more active than the red. That sunlight destroys or diminishes the power or virulence of bacterial poisons is likewise well known.

(*f*) The influence of *atmospheric pressure* on bacterial life has not yet been thoroughly worked out; ordinary atmospheric variations seem to be indifferent. We know, however, that beyond certain depths, or above certain altitudes, micro-organisms cannot be detected with our ordinary means. Regnard has shown that putrefactive organisms are inhibited in their growth and activity by pressures varying from 600 to 700 atmospheres. Albuminous substances which readily putrefy were kept for weeks in a sound condition under such pressures, even when such organisms were known to be present. It is of course possible that, as there are thermophile bacteria which thrive at amazingly high temperatures, there are also organisms which resist such pressure as is found in the lowest depths of the sea.

Summary. — Most of the known micro-organisms can be cultivated on artificial media; but, as already stated, there are many which refuse to grow on such soils, for example, the bacillus of leprosy, the spirillum of relapsing fever, and many spirillar forms which are found in the tissues and in animal secretions or excretions. We must always remember that the artificial media used in the laboratory for the cultivation of micro-organisms are "artificial," and that the phenomena observed under these conditions are evidently not the natural ones. Scientific work, however, could hardly be possible, unless media could be made up for artificial cultivation. Those that are commonly in use may be divided into (1) liquid media, and (2) solid media. The former include broth, milk, urine, blood serum, vegetable infusions; the latter potatoes, meat, gelatine, agar-agar, or coagulated blood serum. It would be beyond the scope of this article to enter into a fuller discussion or description of these various media and their selective advantages; it will be sufficient to say that there is no universal medium, fluid or solid, for all organisms: some, for instance. grow well on agar-agar, and with difficulty on gelatine; others better in liquid than on or in solid media. Many bacteria suffer in an acid reaction, others prefer acidity. Then there are some which grow best on serum or media containing serum, as, for instance, the gonococcus. Such organisms

may often be gradually accustomed to an existence and active life on or in the ordinary media of the laboratory. Thus it has not taken many years to "force" the bacillus of tuberculosis to grow on such ordinary substances as glycerine agar-agar; yet when Koch first separated this bacillus, it was with serum only that he could succeed. Again it is a common experience, on first separating an organism from the living animal, to find that it grows slowly or with difficulty on agar-agar; but if frequently transferred from one tube of agar-agar to another, it will soon become adapted to this soil.

Classification of Micro-Organisms. — These observations, made in the laboratory and at the bedside, in respect to the question of soil have led us to make the following classification —

1. The *parasitic* micro-organisms, which are capable of developing and thriving in living animal tissues.

2. The *saprophytic* micro-organisms, which can live outside living animal tissues, that is, on dead or dying tissues, or on mineral and inorganic substances, or on vegetable matter.

The parasites are again subdivided into (*a*) *obligatory parasites*, and (*b*) *facultative saprophytes*. The former are restricted exclusively to living animal tissues, while the latter, after leaving them, can continue to exist outside the living animal body also — although, perhaps, they only attain full vigour and development when they find their resting-place in the living tissues. Similarly the saprophytes also are classified as (*a*) *obligatory saprophytes*, and (*b*) the *facultative parasites*. After what has been said the meaning of these names is obvious. Now organisms which can be grown in or on the usual laboratory media are not, strictly speaking, obligatory parasites, for they possess the faculty of living on dead matter outside the animal body. Later we shall see that a full grasp of this classification is of the utmost importance in the ætiology, prevention, and hygienic treatment of infective diseases. However, we must realise that we know very little of the natural life and habitat of most pathogenetic organisms; and that often when we argue that certain infective organisms cannot find, or can but rarely find, suitable conditions for growth outside the animal body, we may be arguing from ignorance. More than one organism, once thought to be a true parasite, has gradually been degraded to the less dignified position of a facultative saprophyte or facultative parasite. The tubercle bacillus, for instance, has been shown to grow well on ordinary potatoes, on bread, boiled turnips and macaroni under aerobic as well as anaerobic conditions, at the ordinary room temperature and at blood heat; it is certainly therefore a facultative saprophyte. To this question we shall return.

It must be remembered that organisms found in the animal body are, firstly, not necessarily parasitic; and, secondly, not necessarily harmful. It is true, so far as we know, that the normal blood and tissues do not contain micro-organisms; but micro-organisms are invariably found on the mucous and cutaneous surfaces and near their various outlets. They are

also found in many secretions and excretions, for example, the saliva and fæces, which are readily contaminated with bacteria. Now it is obvious that such organisms are generally either saprophytes or at most facultative parasites. Again, many of these organisms may be of distinct and special benefit to the host. It is well known that plants thrive badly when grown in sterile earth and nourished with sterile food. Similar experiments have not yet been made on the higher animals; but it is probable that an animal kept and nourished under strictly aseptic conditions would thrive as badly as would a plant. Many of the organisms found in the human body — especially those on the mucous surfaces of the alimentary tract — may have become necessary to our metabolic activity. Microbes which are tolerated and harboured by the body, which grow and thrive with it, and seem even to contribute to its welfare, are not parasites, but are said to live with it in *symbiosis;* they are "commensal."

III. Products of Bacterial Activity

The bacteria, while growing in the tissues, or when cultivated in an artificial medium such as broth, remove and use up certain substances for their own nutrition; but they also, by means of their protoplasmic activity, manufacture others which either pass into the broth and are there held in solution, or produce secondary changes in the broth by fermentation or other chemical interaction. It is obvious then that the liquid or medium in which bacteria are growing may become altered (*a*) by the assimilation of nutritive material by the organisms; (*b*) by the products of secretion elaborated and given out by the bacterial cell; and (*c*) by subsequent secondary changes induced by these products.

The sum total of these chemical and physiological changes constitutes all that is included under the term "bacterial products." These products are not necessarily toxic when tested on the ordinary laboratory animals. It will be found that any one pathogenetic organism manufactures a series of substances, of which some are harmless, others poisonous; even these latter indeed are not equally poisonous, but differ in kind and in degree of activity. No doubt the *specific* symptoms and phenomena of most infective diseases are due to *specific* poisonous agents; but we must be careful not to lose sight of the complex nature of bacterial chemical changes which in the body lead to a series of secondary symptoms, no less important perhaps than the more striking *specific* ones. Unfortunately the language of the bacteriological chemist is at present far from exact. The processes of bacterial activity are extremely complex, and until we know more of them, we are compelled to use such general terms as "bacterial products," "toxins," and "virus." For instance, when diphtheria bacilli are grown in a flask of broth, the liquid is said to contain the bacterial products; but many of the substances held in solution by the liquid may not have been primarily produced by the bacteria, but by a secondary fermentative action. Bacteriological chemistry is a young branch of science, and as yet even more backward than physio-

logical chemistry; we shall therefore restrict ourselves here to a few of the more familiar points of theoretical and practical importance.

The assimilated substances are employed (*a*) for the purpose of building up the bacterial cell; and (*b*) for the purpose of manufacturing certain substances which are afterwards discharged from the bacterial cell by a process of secretion or excretion. For us the substances eliminated by the bacterial cells and the secondary products elaborated by these substances from the culture medium are of the greatest importance. We shall first take a general survey of the chemical bodies obtained from bacterial cultures, that is, not from any one culture in particular, but from a large variety of cultures taken collectively: — the scope of bacterial chemistry.

1. *Gases* are formed or given off by many organisms, for example, the anaerobic bacteria, the many varieties of bacillus coli communis, and numerous putrefactive organisms. Among these gases are CO_2, H, CH_4, H_2S and NH_3. CO_2 no doubt is given out by all organisms. Some, however, possess the power of forming gas to such an amount that, when grown suitably in solid media, large gas bubbles will appear in the substance of the gelatine and the agar-agar; and when placed in the animal body, gas will be formed sometimes also in the tissues, to such an extent as to produce an emphysematous condition (some forms of septic gangrene, malignant œdema, "schaumleber," symptomatic anthrax).

2. *Fatty and oxy- acids* and their *amido-compounds* are commonly found in bacterial cultures; for example, acetic, propionic, butyric, and lactic acids and their compounds; also leucin and other amides.

3. Of importance also are the bodies belonging to the *aromatic* series, such as tyrosin, phenol, cresol, which are oftenest found in fermenting and putrefying mixtures.

4. Many organisms are capable of forming *indol*, a substance well known to the physiologist, which is formed almost certainly by bacterial action from proteids by a process of decomposition during their stay in the intestine. It is manufactured by many putrefactive organisms, by the bacterium coli, and numerous choleraic vibrios.

5. Some organisms are *chromogenetic*, that is, they secrete or manufacture pigments. The latter may occasionally be contained in the substance of the organism (intracellular), more commonly in the medium outside (extracellular); sometimes they impart a general diffuse colour to their surroundings, a colour varying in intensity with the medium in or on which the bacteria flourish. The range of colours is very wide. Thus red colouring matter is formed by the bacillus prodigiosus; green or blue by the bacillus pyocyaneus and the bacillus fluorescens; yellow by many sarcinæ, bacilli, and staphylococci; violet by the B. violaceus and the B. ianthinus. The pigment formation depends (*a*) on the nature and consistence of the medium, being most marked as a rule on a solid one; (*b*) on the presence of air and oxygen (thus the bacillus prodigiosus does not form pigment in the depth of a gelatine tube); (*c*) on the temperature (some organisms like the bacillus prodigio-

sus refuse to form their colouring matter in the warm incubator); (*d*) on the activity of the light to which the organisms are exposed (sunlight often prevents colour formation, and may cause the pigment to disappear after it has once appeared).

6. Lastly, there are the *ferments* and *enzymes*, the *ptomaines*, the *toxalbumins*, and the *products of fermentation*. These substances to the pathologist are of the greatest importance, and they are taken together here on account of their close relation, chemical or historical, one to another; also because these bodies stand out prominently among the other bacterial products, often as physiologically or pathologically specific substances which are found only with certain organisms. The bacterial products, as I should have said before, are either general or indifferent, that is, such as are common to all or, at any rate, to a large number of micro-organisms; or specific, that is, such as belong to a few only.

Fermentation is a process by which complex substances are split up into simpler ones. It may be (*a*) purely chemical, initiated and effected by the products of secreting cells; or (*b*) vital, governed by the vital phenomena of the cellular organisms. In the latter case we are dealing with the manifestation of life by the cells; on their death fermentation ceases. The cellular organisms are the true *ferments* as distinguished from the *enzymes* or chemical ferments. The former are destroyed by disinfectants, notably chloroform or thymol, substances which do not affect the activity of the enzymes. Many of the vegetable organisms secrete or form enzymes, while they themselves act as ferments. The yeast cells, for instance, manufacture an enzyme, invertin, which converts cane sugar into dextrose and lævulose; but they themselves act as an alcoholic ferment which changes the dextrose into alcohol. Although most enzymes are discharged outwards, that is, are secreted, and act extracellularly, some of them effect their fermentative action intracellularly, that is, in the substance of the bacterial cell. The micrococcus (bacillus) ureæ is the best known example of an organism, capable of forming an enzyme, acting intracellularly. From the dead bodies of these organisms a substance can be separated which will change urea into ammonium carbonate. It is important thus to distinguish between ferments and enzymes.

Among the *enzymes* the following have been separated or isolated: (1) Diastatic enzymes, which convert starches into glucose or dextr[illegible] have been found in lactic acid bacilli, and in certain intestinal germs. (2) Invertin, an enzyme capable of changing cane sugar into dextrose, is found in intestinal bacteria, in yeast cultures, and in lactic acid bacilli. (3) Many organisms are capable of peptonising proteids, that is, of converting them into albumoses or peptones. The liquefaction of gelatine, a property of a large number of bacteria, seems to be due to peptonisation. (4) The presence of bacteria in milk often produces coagulation or curdling. The bacillus coli communis is one of the most active organisms in this direction. There are other enzymes, as for instance those capable of dissolving cellulose and of splitting up urea, but they are of less importance.

Some of these enzymes have been prepared from bacterial cultures in a more or less pure state. Such enzymes, forming peptones, dextrose, and other substances which remain in solution, must greatly alter the composition of the media in which the bacteria are growing. Peptones and albumoses are the commonest substances found in such albuminous media, as alkali-albumin and serum, and undoubtedly they owe their origin to fermentative processes; of these we shall speak later. Besides manufacturing these specialised enzymes, many of the pathogenetic organisms may act as living ferments, and by complex changes produce specific substances in the media in which they grow, in other words, they may produce fermentation.

We see, then, that in any bacterial culture, as in the case of the yeast cells, two kinds of fermentation may go on at the same time, (*a*) that produced by chemical substances — the secretion of bacteria in this particular case — a process comparable to peptic fermentation; (*b*) that carried on by living organisms. Of this vital fermentation in disease at present we know but little. The best known forms of vital fermentation do not play a part — or but a small part — in disease; they are (*a*) alcoholic (yeast); (*b*) lactic (bacillus acidi lactici); (*c*) butyric (bacillus butyricus); and (*d*) acetic fermentation. Fermentative processes are obviously capable of altering the chemical composition of a nutrient medium in a striking manner.

Neither the ferments nor the enzymes are used up in the processes which they initiate; on the contrary, up to a certain point, the ferment cells multiply in the nutritive solution. The amount of enzymes present must of course depend on the number of organisms. A nominal quantity of ferment cells suffices to produce extensive fermentative changes: this, however, is also true of many enzymes, as, for instance, of some milk-curdling enzymes; roughly, however, the effect produced by the enzymes varies directly as the quantity used.

As fermentation, like putrefaction, is a hydrolytic process, both enzymes and ferments require water to liberate their power; boiling destroys them, so does cooling; and the retention of the products of their activity eventually inhibits and impairs fermentation. Although the enzymes are capable of acting under anaerobic conditions, the ferment cells cannot permanently do without oxygen; yet a temporary reduction of the oxygen-supply will often raise their fermentative activity.

Of the true chemical nature of the enzymes we are ignorant. They are probably proteins, soluble in water but not diffusible, and precipitated by ammonium sulphate and alcohol. In aqueous solution they lose their fermentative properties when heated to 60°–80° C., though when dry they will resist temperatures of 100°–150° C. In glycerine solution they retain their power almost indefinitely. As a rule they are easily carried down mechanically from their solution by various methods of indifferent precipitation, as by calcium phosphate, cholestearin, etc. It is important to keep in mind this readiness of the enzymes to come down on precipitation; because it is quite possible that some of the many discrepancies

which make the subject of bacterial chemistry so perplexing are due to imperfect knowledge of the difficulty of successfully separating the (so-called) enzymes. To this matter we shall come back in a final review of the present position.

The *ptomaines* are certain basic compounds formed by the action of bacteria on dead albuminous substances; they include highly toxic substances which have been compared to alkaloids, and have been called animal alkaloids. As a matter of fact, however, they differ considerably from the vegetable alkaloids, being amines (mostly di-amines); and they are formed most commonly in the early stages of putrefactive processes. Brieger has separated ptomaines from cultures of the typhoid bacillus, the cholera vibrio, and the bacillus of tetanus; and Leber obtained phlogosin from the staphylococcus aureus and the streptococcus pyogenes. These bodies, with a longer series separated from various decomposing tissues, are highly toxic; it was therefore assumed at one time that the characteristic symptoms of many infective diseases are produced by these ptomaines, and the symptoms of many food intoxications and of certain intestinal infections are still attributed to an absorption of these substances from the intestinal tract. Dr. Cunningham, for instance, regards, and possibly with justice, Asiatic cholera as an intoxication by ptomaines formed by the bacteria of that disease.

Without entering deeply into this question, we may take it as certain that there are many pathogenetic bacteria which manufacture no ptomaines; or, at any rate, whose ptomaines when administered to an animal produce none of the specific symptoms associated with the disease; lastly, the amount of ptomaines separable from large and copious bacterial cultures is so very small that in many cases a doubt of the specific importance of these substances is justifiable. Moreover, many of Brieger's specific ptomaines have not stood the test of time — for example, his tetanin, spasmotoxin, and tetanotoxin, on which, indeed, he himself has turned his back. Sidney Martin found an alkaloidal basic body in anthrax cultures, and in the tissues of animals dead of anthrax; but it was always accompanied by other toxic substances. In most cases chemical analysis has failed, with new methods in competent hands, to detect specific ptomaines. No doubt many of the ptomaines, where found, produce injurious effects; but before we can concede much importance to them we must be satisfied that they are capable of reproducing the characteristic symptoms. Anyhow, it seems that at present the ptomaine theory has lost ground, and in many quarters has been given up — it was merely a phase. Undoubtedly ptomaines exist, often appear during early decomposition and putrefaction [see article on "Ptomaine Poisoning"], and are found in certain cases of food-poisoning and in some forms of disease; but it is erroneous to put down all bacterial toxins as ptomaines. Two further matters may be mentioned in this elementary sketch, namely, that not all ptomaines are poisonous.[1]

[1] Brieger in his classification applies the term "toxins" to the poisonous ptomaines, the term "ptomaines" to those which are not poisonous — a useless method of classifying

and also that some ptomaines are extremely resistant to high degrees of temperature.

With the discoveries of toxic albumoses in bacterial cultures, by Mr. Hankin and Dr. Sidney Martin, the ptomaines were more or less lost sight of, and fresh paths of research were opened up. Weir Mitchell and Reichert had already shown that the toxic principles of snake venom are albuminous substances; they supposed them to be mostly toxic peptones. Later it was demonstrated that they are not peptones but albumoses. Others followed up these researches, and of great importance were Sidney Martin's investigations on abrin, which he also proved to be a toxic albumose. Indeed it soon appeared that a fairly large number of highly, and even intensely poisonous substances, whether derived from the animal by glandular activity, or from seeds of plants, or from bacterial cultures, owe their toxic properties to albumoses. Hence these peptone-like substances came to be regarded as the specific poisons of pathogenetic bacteria, and this the more as they were obtained from a series of organisms. When Roux and Yersin had precipitated the active principle from diphtheria cultures, which they called an enzyme; and when Brieger and Fränkel, working with different methods, had come to the conclusion that the diphtheria toxin is an albuminous body, or a "toxalbumin," Sidney Martin showed that from diphtheria cultures in alkali-albumin toxic albumoses can be obtained which, injected into a guinea-pig or rabbit, produce all the classical lesions of the disease. But, before Martin's researches, chemists had already suspected that the diphtheritic toxalbumins of Brieger and Fränkel were really albumoses. Albumoses have also been found in cholera and pneumococcus cultures, and in Koch's tuberculin. Gradually, however, it became evident that many of the bacterial toxins do not react as albumoses, but that some answer to peptone tests, others behave more like globulins, and so forth. It seemed, then, that from bacterial cultures various kinds of poisonous albumins or proteids or albuminoid bodies may be separated, and hence the general term *toxalbumins* was applied by Brieger and Fränkel to all of them.

It is quite true that from several bacterial cultures (B. anthracis and B. diphtheriæ) toxic albumoses can be separated, if the organisms be grown on an alkaline serum free from peptone; and these albumoses, when injected into the animal body, will produce the lesions characteristic of anthrax and diphtheria: but it is equally true that specific albumoses are not to be obtained from all pathogenetic bacteria. If, however, we use the more general name toxalbumin in the sense defined above, it may be said that specific toxalbumins have been found in anthrax, diphtheria, pneumonia, in almost all infective diseases, and in most cultures of pathogenetic bacteria. Toxalbumin, however, is an inaccurate name, since it would include practically only the true albumins and the globulins, and would exclude the proteins (nucleo-albumins) and the albuminoid substances.

Now the albumoses and peptones which constitute so important a series among the bacterial products may be derived by hydrolytic processes from

any one of those albuminous or albuminoid substances including the nucleo-albumins; and, strictly speaking, they are not covered by the name albumin. It is better, therefore, to follow Neumeister, and to speak of toxic *proteins*, which designation includes the albumins, the proteids, and the albuminoid bodies. Taking this wider view, we shall meet with fewer difficulties than if we restrict ourselves to the terms toxalbumins or to albumoses. In the case of snake venom, for instance, we find that their composition is anything but uniform; some contain toxic globulins, others albumoses, primary and secondary, others perhaps peptones [*vide* art. on "Snake Poisoning"]. In abrin, again, there are both an albumin and a globulin; toxic proteins exist also in ricin and other similar substances; and we have seen that the nature of the bacterial products may vary considerably.

Many of these proteins may be precipitated in an amorphous form from the culture medium in which the bacteria grow; when in solution they are generally readily destroyed by heat (snake poison, however, less readily), and are rendered atoxic by the action of the digestive secretions. In a dry state, like enzymes, they resist heat better; and they often resemble the enzymes in this also, that they set up their toxic effects when injected in extremely minute doses; so that they would seem to act not directly on the tissues, but, after the manner of enzymes, to produce a kind of toxic fermentation.

Summary. — We have seen that by Brieger's researches the attention of the scientific world was directed towards the poisonous ptomaines, but we soon learnt that the part which these play in infective diseases can only be one of secondary importance; next we were taught to look for the secret of these diseases in toxic albumins, albumoses, or, in short, in toxic proteins, that is, in substances reacting like proteins (albumins, globulins, albumoses, etc.), which cannot be chemically distinguished from ordinary known proteins, but are endowed with toxic properties. Duclaux and others, however, have raised a protest against this view, and have always assumed that the toxo-proteins in reality are mixtures of albuminous, proteid, or albuminoid bodies with the true toxins, the latter being carried down mechanically during precipitation; and recent researches have shown that, if for the purpose of cultivation a non-albuminous solution be employed, the result is not an albumose or a globulin or a toxalbumin, but an indefinite body, perhaps albuminoid in nature, and allied to the enzymes and ferments. Brieger and Cohn have demonstrated that it is possible to purify the toxin of tetanus (which, when obtained from broth, appears to be a toxalbumin) in such a manner as to rid it more or less completely from all the albuminous and albuminoid substances clinging to it; and Sidney Martin, although his researches are as yet unpublished, has confirmed this in a most striking manner. He has shown the presence of albumoses in tetanus cultures, which, however, are simply pyrogenetic in their action; the true toxin which is obtained after the removal of the toxalbumins is not an albumin, nor a proteid, nor of course a ptomaine.

We see then how obscure the whole subject still is, and that the name given to a bacterial toxin apparently varies within certain limits with the culture medium used. The albumoses are supposed to be formed by a process of fermentation, the bacterial cell secreting an enzyme which, acting on the albumin in the culture medium, splits it up into albumoses; as the peptic cells in the gastric mucous membrane secrete the pepsin which, acting on the proteids in the stomach, converts them first into albumoses. However tempting this opinion may be on account of its simplicity, in the light of more recent researches it can hardly be regarded as conclusive. Most investigators, while preparing the toxins from bacterial cultures, use media which already contain peptones or albumoses; we do not wonder then that, on precipitation with alcohol or ammonium sulphate, they obtain toxic albumoses, or in short toxalbumins. True. Sidney Martin used a medium free from albumoses and peptones, but containing alkali albumin; and on growing anthrax and diphtheria bacilli in such a solution he eventually obtained toxic albumoses: it would seem then that these bacilli either act as ferments, or secrete enzymes, which change the alkali albumin into toxic albumoses. So far as diphtheria is concerned, he inclines to the view that its bacillus secretes an enzyme; for out of the diphtheritic membranes a proteid substance may be extracted which does not give albumose or peptone reactions, and yet produces the same effect on the animal as the albumoses, though administered in much smaller doses. Martin therefore argues that the bacilli set free an enzyme which, by hydrolysis, converts the albumin into albumoses, which latter, acting as poisons, produce the true diphtheritic lesions in the animal. He finds also that they form identical substances (albumoses) from the proteids of the human body. "It may be," he says, "that the chemical substances which are especially poisonous are produced by means of an unorganised ferment (that is, an enzyme) secreted by the bacillus, and in diphtheria there is evidence to show that this enzyme plays a direct and important pathological part. In this disease, in which the bacillus is limited to the superficial parts of the membrane, and does not diffuse itself throughout the body, something is secreted by the bacillus and then absorbed into the system, in the tissues of which are afterwards found certain digested products (that is, albumoses)." This secretion of the bacillus may be looked upon as an enzyme; so that Martin's conclusion is that the bacillus diphtheriæ liberates an enzyme which digests the proteids of the body or of the culture medium, forming toxic albumoses, and that the latter produce the characteristic morbid changes. The toxic diphtheria products in the body do not all come directly from the membrane, the albumoses do not merely accumulate in the tissues; it is more probable that the enzyme, absorbed from the membrane, by digesting the tissue proteids forms toxic albumoses. Martin gives a useful table, which is here reproduced in slightly altered form, to contrast the chemical pathology of anthrax and diphtheria with the physiological processes of peptic and tryptic fermentation:—

Digestion Process.	Origin of Enzyme.	Ezyme.	Products of Fermentation.
Peptic.	Peptic cells.	Pepsin.	Albumoses. Peptones.
Tryptic.	Pancreatic cells.	Trypsin.	Globulin-like body. Peptone.
Anthrax.	B. anthracis.	. . .	Albumoses. Peptone.
Diphtheria.	B. diphtheriæ.	Enzyme of Roux and Yersin, and of Martin, found in membrane.	Albumoses.

Martin does not fall into the error of applying this scheme to all infective organisms alike; he shows that the albumoses which may be separated in the case of tetanus, though not innocuous, do not possess the specific characters of the tetanic poison; and, as above mentioned, the toxin of tetanus is not an albuminous or proteid substance. Yet, so far as diphtheria and anthrax are concerned, his views undoubtedly are that the pathogenetic bacteria are capable of digesting proteids in such a manner as to produce the agents which set up the symptoms in these infective disorders. This conception of the problem is very tempting, but it is also beset with difficulties. Thus the proteolytic action of the so-called diphtheria enzyme has never yet been demonstrated; this so-called enzyme may be the true toxin which is diffused throughout the body at the same time as albumoses are formed, and on precipitation the two substances may be carried down together [*vide* art. "Diphtheria"]. In tetanus, certainly, the albumoses are of secondary importance.

But the greatest difficulty is presented by the researches of Uschinsky and Buchner. The latter excluded albuminous substances from their culture media by using solutions containing asparagin and mineral salts; and on growing tetanus and diphtheria bacilli in such solutions, they obtained the active and specific toxins of tetanus and diphtheria as bodies clearly allied to the albuminoid substances, but not classifiable or definable except by their reactions. They are therefore disinclined to accept the view that the bacterial poisons are formed by a fermentative action from the albuminous substances of the body or culture media: they regard them as direct products of the bacterial cells, that is, as direct derivatives from the cell plasma, which, as such, must necessarily share the specific properties of the bacterial cell whence they came. As yet it has been impossible to separate these substances from albuminous solutions in a pure state, because all the reagents which precipitate them will also carry down simultaneously the albuminous and proteid bodies contained in those solutions. Buchner does not picture to himself the action of

these toxins as a fermentative one, chiefly perhaps because within certain limits the rapidity and the intensity of the effect produced vary with the dose administered. Yet it is a striking fact, of which we can readily obtain evidence, that many of the bacterial and animal toxalbumins produce fatal lesions in minute doses; and, what is still more wonderful, that a so-called minimal lethal dose will often be followed by no manifest signs or changes for some days, and then after a period of latency symptoms of astonishing acuteness may suddenly appear; and, lastly, that "sublethal" doses frequently lead to slow wasting, exhaustion, prostration and death. It would be useless with our present knowledge to speculate on the meaning of these phenomena, to which there is no analogy in ordinary toxicology. We cannot as yet answer the following questions — whether the toxins are themselves the poison, or whether they are poison-producing enzymes; or again on what the prolonged slow action of the toxins under special conditions depends. In the case of enzymes, such as pepsin and invertin, we must carefully distinguish between their fermentative and their toxic actions. When injected into the animal body they produce rise of temperature, general disturbances and death, acting not by means of fermentation, but as direct poisons.

To come back to the chemical nature of the toxins; we have seen that during the fermentative changes produced by the bacteria, besides the direct products of fermentation, there are other substances also which we may regard as the secreta or excreta; that is, as the metabolic or waste products of the bacteria. In most cases it is difficult to say with certainty what they are. This, however, is important: "If an organism growing in various media *always* produces certain definite substances, then we are forced to consider these to be the genuine metabolic products." Now we find, for instance, that if the cholera vibrio be cultivated on different media, we can extract a series of substances different in their chemical reactions, but all identically toxic. Naturally the fermentation processes must vary with the nutrient medium employed, and their reactions can only be complete with certain special media; but, nevertheless, the metabolic products appear to remain physiologically and pathologically constant: so we may conclude with Wesbrook that the choleraic toxin is the constant, associated either with the proteins of the nutrient medium or with the products of fermentation. This seems more reasonable than to assume that the vibrio may form different chemical toxins with constant physiological or pathological properties.

This vibrio forms an interesting illustration of the continual change of our opinions. Brieger described no less than six ptomaines, all toxic, but none specifically so; Scholl, growing the vibrio in eggs, obtained a toxopeptone; Gamaleia extracted poisonous substances from the bodies of the dead bacteria, which he classified as nucleins and nucleo-albumins; Voges also sought for the cholera toxin in the bacterial cell, and regarded it as an enzyme, since when obtained from suitable media it reacts neither as an albumin nor albumose nor peptone. Duclaux, as previously stated, consistently refused to regard the bacterial products as true proteins, but

argued that they are special bodies of unknown nature, mechanically carried down during precipitation, or perhaps forming compounds with the proteins. This view of Duclaux has much in its favour; the chemical evidence, however, is still wanting: fresh observations are needed. In the meantime we may sum up that among the specific toxins there have been found (*a*) ptomaines, (*b*) toxic proteins, toxalbumins, (*c*) nucleo-albumins and albuminoid substances, (*d*) ferment-like bodies (enzymes) secreted by the bacterial cell; and knowing as little as we do, it is safest to apply to the bacterial poisons the general term *toxin*.

Matters have not been made easier by Dr. Klein's division of these poisons into (*a*) intracellular and (*b*) extracellular poisons. Klein has shown that the protoplasm of the bacterial cells is often highly poisonous; and argues, therefore, that many bacteria contain poisonous substances in their protoplasm (intracellular poisons). These, as a rule, he says, produce none of the specific symptoms; but when injected into the animal cause inflammation, suppuration, and often death. They must be distinguished from the "extracellular" poisons formed by a fermentative or other action on the culture medium, the extracellular poisons being the true specific toxins. Thus, to give an example, the diphtheria bacillus, acting on the surrounding albuminous medium or animal tissue, forms its toxic albumoses, that is, "the extracellular specific poisons," which cause the classical symptoms of the disease; while within itself the diphtheria bacillus contains the "intracellular non-specific poison." Chemical analyses of the bacterial protoplasm were made before Klein by Nencki, who obtained from putrefactive and other organisms albuminous or albuminoid bodies which he called mycoproteins. These resemble the true albumins, but are nevertheless essentially different in their reactions. These mycoproteins undoubtedly correspond to Klein's intracellular poisons.

Buchner approaches Klein very closely in some of his views. He also distinguishes between "bacterio-proteins" (not to be confounded with Nencki's mycoproteins) (that is, mycoproteins or intracellular poisons) and the specific amorphous toxins, which, however, he also associates closely with the cell protoplasm. The former are common to many bacteria, are more resistant to heat, and when injected into the animal body produce inflammation, suppuration, and fever. According to Buchner, then, both the bacterio-proteins and the specific toxins are intracellular poisons; and this seems, for the present at least, the soundest view to accept, because if, for argument's sake, we were to accept Klein's view, we should find that the virulence of his so-called intracellular poisons varies, as a rule, directly with that of his extracellular poisons. Again, immunity from the intracellular poisons generally, if not always, implies also immunity from the extracellular poisons. It would take us too far, nor is it necessary at present, to discuss these views more fully; I must content myself with this short mention of them. I may, however, allude to recent researches on yeast fermentation, which show that as the yeast cells themselves always contain alcohol, it is quite possible that the formation of

alcohol is an intracellular process; the alcohol, which is the analogue of the toxin, being secreted or excreted by the cells into the surrounding medium.

Fuller accounts of the various toxins will be found in special articles. Here we can admit only a general summary of a subject full of speculations, and open to many fallacies due to personal bias and to the present defects in our knowledge of physiological chemistry. The chief lesson to be derived from the study of bacterial toxicology is this, that the characteristic symptoms of any infection are due to toxins; therefore in our study of microbic disease our aim must be to establish the specificity of the bacterial products. Thus while dealing with a disease, such as tetanus, which is readily recognised by strikingly characteristic symptoms, we must show, not merely that these symptoms are produced by injecting the bacilli of tetanus, but that the toxins (or sterilised cultures containing the metabolic products in solution) will produce the same symptoms; in other words, that the toxins and microbes are alike specific. This has already been done for tetanus, diphtheria, and anthrax. We find, then, that the pathogenetic bacteria produce poisons, whatever their chemical nature may be, which, on obtaining entrance into the animal body, will cause the appearance of the specific symptoms of the disease under consideration.

We have seen that the various substances, toxic and atoxic, produced by bacterial life, are manifold; and that any one organism may, and probably does, form a number of them, partly by secretion or excretion, and partly by fermentation. Thus we may explain the complexity of the symptoms of infective diseases, the specific symptoms being caused by the specific poisons, and the concomitant symptoms by the other substances formed by bacteria and bacterial fermentation. We must always remember that as the chemical processes and their products are far from simple, their effects must likewise be complex.

The fermentative action, real or apparent, of the pathogenetic bacteria and their products is then perhaps their most striking and important property — at least in all general infective lesions; the organisms themselves acting partly as ferments, partly as zymogenetic cells. The toxins often resemble enzymes so closely that the general opinion inclines to place all these bodies in one and the same chemical group, not as identical but as allied bodies. Hence, wherever in nature we find fermentation, real or apparent, the presence of living micro-organisms must be suspected; though of course we must not forget that certain zymotic or fermentative processes appear to be independent of bacteria, as, for instance, intoxication with snake poison. Organisms capable of initiating and completing fermentation have been called *zymogenetic*; and since many morbid processes are analogous, if not akin, to fermentative processes, and are, moreover, produced by organisms, the term *zymotic* has been applied to them, — a term, however, to be avoided rather than recommended.

Though we cannot enumerate and discuss all the various complex

chemical and physical changes which micro-organisms in general are capable of producing in their surroundings, allusion must be made to a few other important, or at least highly interesting phenomena of bacterial activity, such as the processes of nitrification, putrefaction, and production of light.

(*a*) *Nitrification* takes place especially in the soil and in water, and is one of the most important and essential processes for organic, and especially for vegetable life. In the soil, where it has been more carefully studied by Winogradski, Frankland, and Warington, two separate changes are said to take place. (*a*) Some organisms decompose ammonia into water and nitrous acid; (*β*) others, though powerless over ammonia, oxidise nitrites to nitrates, and in that way supply the nitrogenous food to chlorophyllous plants.

Conversely many bacteria possess the power of reducing nitrates to nitrites; others are capable even of absorbing free nitrogen. All these organisms are of the utmost importance in the vegetable economy, as they assist the growing plant and the germinating seed to obtain the necessary supply of food. These organisms collectively complete the processes of putrefaction by converting the ammonia first into nitrous acid, and the nitrous compounds further into nitrates, in the presence of basic substances. The nitrates are then again reduced to nitrites and ammonia, and so on. The cholera-vibrios possess the faculty of forming nitrites, while many bacteria found in fæces are capable of still further reducing the nitrites to ammonia. There is reason to believe that bacteria are as important to animal life as they are to plant life; experiments on lower animal forms prove this, and the laws of adaptation would lead us to expect it.

(*b*) *Putrefaction* may be roughly considered as a form of fermentation of albuminous and albuminoid matter. The whole chemical process of putrefaction is too complex to be considered here; a few words must suffice. It seems that the first change is peptonisation, effected in part by the peptonising enzymes possessed by most organisms of decomposition. The peptonised substances are then further changed and split up; amido-derivatives (especially amido-acids), aromatic bodies, and sulpho-acids are next formed, and these are further split up, indol being among the final products. The list of substances which may appear during putrefaction is very extensive; it contains among the gases CO_2, H, H_2S, and CH_4; among the fatty acids acetic, butyric, and valerianic acids, besides various amido-compounds — amines, indol, skatol; bodies of the aromatic series; various ptomaines; basic compounds, etc., the chemical combinations varying qualitatively and quantitatively with the particular bacterial species concerned, and with the decomposing medium. The result of putrefaction in all cases is the decomposition of highly complex substances into others of simpler and more assimilable structure. It is especially under anaerobic conditions that the odour of putrefaction is observed.

The list of putrefactive organisms includes various forms of proteus

(vulgaris, mirabilis, Zenkeri), for which formerly the name bacterium termo had to do duty, and also a large number of other aerobic and anaerobic bacteria, many of which are still without proper names.

(*c*) The *phosphorescence* observed on the surface of sea-water, or on decomposing meat or fish, is due to photogenetic bacteria, of which there are many varieties. This curious and beautiful effect depends on active oxidation, and the phosphorescence disappears in the presence of CO_2.

Our observations on bacterial products must be concluded here, for in a general introduction it would be out of place to enter into matters which are either doubtful or of importance rather to the specialist than to the physician. The latter will find no difficulty in appreciating the excellent warning of Professor Welch, who says that "in fixing our attention upon the poisonous chemical products of bacteria we must not lose sight of the fact that these are results of *vital* activities. In the case of most infective diseases we can no more dissociate the actual presence, multiplication, and specific vital activities of the bacteria within the body from the disease than we can substitute any chemical substances for the actual presence and growth of the yeast fungi in the production of alcohol from sugar. We cannot resolve bacteriology into toxicology."

Variability of Virulence. — As the shape and forms of bacteria may vary or may be altered by changes in their surroundings, so likewise may their physiological, chemical, or vital activity be greatly modified — often to such an extent that in many cases we seem to come very near new species. Thus, as said above, many chromogenetic organisms lose their power of forming pigment under special conditions; among these conditions are absence of oxygen, increased temperature, insolation, and change in the chemical reaction of the nutrient medium. In some cases by such interferences we may obtain varieties which, if they do not remain permanently colourless, at any rate have become incapable of pigment production for many generations, or — to express it differently — show no reversion to the chromogenetic type for a long time. Similarly modifications may be brought about in the fermentative activity of bacteria by change of soil or by continued growth on ordinary laboratory media. Thus organisms which at first liquefy gelatine may lose this power permanently; conversely organisms which at first were incapable of liquefying gelatine gradually and permanently acquire this quality. Lauder Brunton and Macfadyen mention a curious instance of adaptation, if such it may be called, while discussing the observation that bacteria which form a peptonising enzyme on proteid soil can produce a diastatic enzyme on carbohydrate soil.

Loss of virulence — that is, impaired toxin formation or impaired metabolic activity — is not only the most important change, but also that most frequently observed. Thus the pneumococcus, if continuously grown on ordinary media, very soon ceases to be virulent, and this loss of virulence is permanent: similarly the diphtheria bacillus on agar-agar

soon becomes less virulent. This loss of virulence is called *attenuation*, and it may be brought about in many ways besides prolonged cultivation in or on artificial media, as by heat, evaporation, drying, chemical dilution, or the addition of chemical substances to the culture media: these methods, however, require no further consideration. Attenuation may be temporary or permanent, as in the case of anthrax, where the loss of virulence is, moreover, accompanied by loss of spore-formation. It is often found also that an organism obtained from a bacterial lesion of severe or malignant type soon loses its virulence, or is from the outset less virulent than an organism separated from a less severe case of the same lesion. The streptococci are in this respect, perhaps, the most variable of all germs, and therefore the most annoying to the active worker. This variability in virulence cannot be satisfactorily explained at present; but it must necessarily lead us to be cautious in our attempts to interpret vital phenomena by means of test-tube reactions only.

The virulence of many organisms may also be permanently or temporarily increased, either by changing the composition of the nutrient media in or on which they grow, or by passing the organisms through a series of animals (a process which is called "*passage*"), especially if the animals be relatively insusceptible. In some cases, however, continued *passage* will lead to permanent attenuation; an important observation in so far as it helps to throw light on the natural decline of many epidemics, which may cease by virtue of a gradual attenuation brought about by continuous transmission from man to man.

It would take us too far to discuss the question of natural races or varieties; indeed, our observations and premises are not exact enough to give us much confidence in so doing. Most writers assume the existence of natural non-virulent varieties in the cases of the organisms of cholera, typhoid, diphtheria, pneumonia, and traumatic infections. These, under special conditions — unknown to us — may acquire virulence either before or on gaining access to the body, and will then be capable of producing the lesion proper to each. This is possible, if not probable: it is safer, however, to suspend our judgment for the present.

IV. Bacterial Activity in Disease

Having considered the products of bacterial activity in general, we can now approach the all-important question of the relation of microorganisms to disease. No one doubts any longer that a number of diseased processes are due to bacteria, and the epithet **pathogenetic** is applied to all organisms capable of producing a morbid lesion in the animal body.

The term pathogenetic is, however, a relative one, because — (1) An organism quite harmless to one animal may be capable of causing disease in another; (2) an organism which, under ordinary conditions, is harmless, under special conditions may give rise to serious lesions; (3) many

organisms, generally regarded as harmless saprophytes, under special circumstances of experiment may prove injurious.

Thus Dr. Klein has shown that the bacillus prodigiosus, which by all bacteriologists is considered not to be pathogenetic, when injected into the peritoneal cavity of a guinea-pig may cause a fatal peritonitis: Buchner, again, has shown that the dead bodies of bacteria, subcutaneously injected into animals, will produce suppuration. We must bear such observations clearly in mind; and we must further remember that often an organism, unable by itself to initiate any morbid change, may, with the assistance of another organism, or in conjunction with it, cause most serious mischief: conversely, the pathogenetic power of some organisms may be counteracted by the presence of another organism.

The lesion produced by so-called pathogenetic organisms may be (*a*) local or general; (*b*) specific or non-specific. If it be local the organisms remain *in situ*, multiplying there rapidly or slowly, and forming their toxins, or setting up fermentative processes. The poisons, secreted by the organisms or formed by the action, fermentative or otherwise, of the organisms on the tissues, are absorbed, and lead to special symptoms and constitutional disturbances; or they may react locally on the tissues, causing necrosis or destruction. The constitutional symptoms produced in such a case may be as serious as, or more serious than, those of a general infection. A few examples will illustrate these points.

In diphtheria and tetanus we have examples of local infections by pathogenetic organisms, accompanied by severe general disturbances. The bacilli of diphtheria generally, and those of tetanus always, remain at the seat of infection, multiplying quickly in the case of diphtheria, and slowly and to a limited extent in the case of tetanus. Both manufacture deadly toxins, which, as they are absorbed or enter the circulation, produce the serious symptoms of the respective diseases. In an ordinary suppuration we have, again, an instance of a local lesion produced by pyogenetic organisms. Here, however, the general intoxication is usually less severe; but the local changes may be extremely severe, and end in ulceration or necrosis.

If the bacterial lesion be a general one, the organisms will be found everywhere in the blood, tissues, and lymph channels; that is, a "septicæmia" occurs, using that word in its stricter pathological sense, and not giving it a clinical meaning. In these cases the poisons and toxins are manufactured in the blood itself, and the intoxication may therefore be very serious. At the same time the mechanical presence of bacteria in the vessels, leading to vascular obstruction or embolism, may act deleteriously. A lesion which is usually a local process, for some reason or another may become general. Thus suppuration may at any time be followed by a general septicæmia, the pyogenetic cocci circulating in the vessels; similarly, a pneumonia may be followed by infective endocarditis, and this again by a general septicæmia. Tuberculosis also may suddenly become general, often after operative interference. We find that the less susceptible an individual to any particular

microbic lesion, or the greater the toxic power of an organism, the less are the chances of a general diffusion. Man, for instance, being comparatively resistant to anthrax, when infected with this bacillus will suffer, as a rule, from malignant pustule only. These matters are also of some importance inasmuch as they concern both prognosis and diagnosis. If, for instance, in the case of pneumonia, diplococci are found in the blood, the prognosis is very grave; similarly if, in the course of tubercular disease, tubercle bacilli appear in the circulation, or if, after a wound infection, pyogenetic cocci appear in the blood, death almost always follows. So far as diagnosis is concerned, the presence of microbes in the blood in diphtheria, endocarditis, typhoid fever, or other diseases, always implies general septic complications.

specificity of disease. A far more difficult question is that of There are certain pathological lesions, characteristic in their appearance and nature, the symptoms of which stand out so distinctly, that they may be recognised at once. If these depend on the presence and action of a particular organism, an organism invariably associated with them, they are called "specific"; and they are said to be due to specific pathogenetic organisms. Thus tetanus is a specific disease, accompanied by unmistakable signs and symptoms, and it is invariably caused by one and the same organism, the bacillus of tetanus. Without this bacillus there can be no tetanus; and it is only the ignorant who, using a loose terminology, still speak of "idiopathic" tetanus. Similarly tuberculosis, actinomycosis, leprosy, glanders, anthrax, typhoid fever, gonorrhœa, and diphtheria are specific diseases. These lesions are severally due to one particular organism, which is essential. Although many, if not the greater number, of bacterial diseases are specific in this sense, it is erroneous to assume, on the other hand, that all of them are specific. Undoubtedly the same morbid lesion may be produced by several different micro-organisms. Thus, ulcerative or infective endocarditis is a distinct disease, characterised by certain pathological and anatomical changes, and often therefore regarded as specific; yet it may be produced by a number of organisms, among which we may mention the various pyogenetic staphylococci and the streptococci of suppuration, erysipelas and pneumonia. [*Vide* art. "Infective Endocarditis."] Strictly speaking, then, there is no specific organism of infective endocarditis; any one of a number of cocci may produce a disease, bacteriologically different from, but anatomically, pathologically and clinically identical with that produced by another member of the same group of organisms. Similarly suppuration may be produced by any one of a large number of bacteria; and in the malady clinically recognised as erysipelas, instead of the streptococcus of erysipelas, other organisms may often be found. Septicæmia and pyæmia, again, may be produced by more than one kind of bacterium, and the same applies to pneumonia. We see then that the same pathological process may be brought about by various organisms; in other words, we may have clinical or pathological identity without bacteriological identity. This observation applies especially to those more general pathological conditions,

such as simple inflammation, cellulitis, suppuration, septicæmia; the more specialised the process the more likely are we to find a specific organism. These are matters of the utmost importance, because they explain the opposition, frequently rather imaginary than actual, which often exists between the physician and the pathologist. A particular name is associated with a set of phenomena which constitute a certain disease, and this name has been applied to the disease before anything was known of its pathology, or anything suspected of its bacteriology. Subsequently it is found impossible to adapt the pathological and bacteriological facts to the narrower or wider signification of the clinical name. The bacteriologist finds that a clinical process or set of phenomena may be produced by more than one kind of micro-organism; clinically the results may be indistinguishable, though bacteriologically diverse.

Again a specific organism, when it finds access into the animal body, will always produce the same lesion; for example, the tetanus bacillus will invariably produce tetanus. But we find that the bacteria which are said to cause some of the so-called specific diseases are by no means specific in their action. Thus the pneumococcus is said to be the specific organism of pneumonia, yet we find that in some cases it will produce a fibrinous inflammation, in others œdema, in yet others suppuration, ulcerative endocarditis, cellulitis, or septicæmia. Similarly the pyogenetic organisms vary considerably in their action. We must, therefore, be extremely cautious in the employment of the term "specific," and must adhere to strict definitions. Recent experiences of cholera have taught us that the specificity of Koch's comma bacillus was a dream, and that a large number of different vibrios are found in this disease.

The interaction of various organisms is another matter of serious importance which has attracted attention during recent years. In many infective processes we always find two or more organisms in symbiosis; that is, we have concurrent infections by several organisms. Thus in pneumonia we invariably find pyococci and the bacillus coli communis in the company of the pneumococcus. And it has frequently been shown experimentally that a non-pathogenetic organism (that is, an organism which does not possess the power of producing specific or non-specific morbid changes when placed in the tissues) is often rendered deadly when another, perhaps equally non-pathogenetic organism is introduced at the same time: we also know that the virulence of many pathogenetic organisms is often increased or decreased by the concurrent inoculation of another organism, which again may be non-pathogenetic. This shows how erroneous a popular impression may be, and how relative a term "specificity" really is. This interaction of micro-organisms has not as yet been sufficiently studied, and here this brief allusion must suffice; I shall revert to this matter presently. It is certain that if in certain lesions the same collection of organisms is constantly found, we may be led astray if we fix on one of them as specific, and neglect the others as contaminations. A study of the correlation and interaction between the various organisms frequently or almost invariably found together, may

in future explain many clinical facts and observations which as yet bacteriology has not explained.

A pathogenetic specific germ must fulfil the following conditions: (*a*) it must be a parasite or a facultative parasite; (*b*) it must be found invariably in the tissues of an animal dead from or affected with the disease in question; (*c*) it must never under any circumstances occur in other diseases, nor within the normal tissues; (*d*) the organism transmitted from the diseased or dead animal to an unaffected susceptible animal must reproduce the lesion, and in this second diseased animal the original organism must be found; (*e*) if the organism can be cultivated outside the animal body, then an artificial cultivation inoculated experimentally into a susceptible animal must again produce the disease, and this animal must again contain the organism in its tissues or blood; (*f*) these processes must occur in invariable succession under identical conditions; (*g*) the toxins and poisonous substances obtained from the artificial cultivations must agree chemically and physiologically with those obtained from the diseased animal.

Unless all these conditions are fulfilled the evidence of the specificity of a given organism is incomplete. In laboratory experiments considerable research is often required to establish all these points, because even the mode of inoculation frequently alters results; moreover it is not always easy to find a suitable susceptible animal, or to find the method of artificial cultivation most adapted for poison formation; the need of some concurrent inoculation may also have to be considered. Another difficulty arises when, in the absence of experiments on man, it is impossible identically to reproduce the disease in another species. This, however, cannot always be regarded as an insuperable objection, if it be remembered that the same organism or the same toxin may, under various circumstances, produce different naked eye lesions, that is to say, different phenomena of a like morbid process.

It will be well here to give a list of the various infective diseases in man, at the same time stating how far their bacterial pathogenesis has been proven:—

1. All the conditions just enumerated have been fulfilled for *anthrax*, *diphtheria*, and *tetanus*, chiefly through the brilliant work of Dr. Sidney Martin, who was the first of pathologists to establish the toxic specificity in addition to the bacterial specificity previously demonstrated.

2. The bacterial specificity has been satisfactorily settled for the following diseases: *glanders*, *tuberculosis*, *actinomycosis*, *gonorrhœa*, and *malignant œdema*. Specific organisms have been separated and the disease has been artificially reproduced in animals. All the conditions excepting the chemical agreement of the disease and the organism, have been fulfilled.

3. The next group includes those diseases with each one of which a certain organism is always associated, an organism which can be cultivated, and which is restricted to its own disease; the successful animal

experiment, however, is wanting. In this group we have *typhoid fever, influenza, mycetoma* or *Madura disease.*

4. The proof is still incomplete in the case of *leprosy* and *relapsing fever,* — diseases which are characterised by the invariable presence of easily recognisable organisms, which are not associated with any other normal or morbid processes. These organisms, however, have not yet been grown outside the human body; but so far as relapsing fever is concerned, artificial inoculation of human blood into monkeys has been successful: in leprosy, on the other hand, experimental infection from man to animal, or from man to man, has not been achieved. Arning's well-known experiment brought, apparently, the desired proof that leprosy may be successfully inoculated from the diseased to the healthy individual; it has, however, no scientific value, since it was performed on a native of an area where leprosy is endemic, and whose relations had leprosy; so that before the experimental inoculation was performed he must have been freely exposed to the risks of infection. For such an experiment to have any value whatever it must be performed on an individual clear of taint, living in a country where leprosy does not occur. On the other hand, a large number of inoculations with leprous material have been practised on man in Europe without a single success.

Although in the last three groups of bacterial diseases the chain of evidence is not quite complete, yet the constant and exclusive association of characteristic organisms with morbid processes equally characteristic, compels us to believe in their specifically infective nature.

5. There are a larger number of infective lesions which are not specific in the sense defined above, — lesions, that is, which may be produced by more than one species of micro-organism, or by several members (varieties) of a definite group of organisms. The various organisms in each of these cases are pathogenetic and do produce, but do not always reproduce, disease in the animal on inoculation. Clinically there is often no difference between the disease caused by one organism and that caused by another. In this group are the various forms of inflammatory and suppurative lesions: *pneumonia, osteomyelitis, septicæmia, pyæmia, endocarditis, meningitis, erysipelas, angina Ludovici, bronchopneumonia,* indeed, the various forms of infective inflammatory, suppurative, or septic lesions which at present we are unable clinically to distinguish by their bacterial flora.

6. *Cholera* is an infective lesion, produced by a number of vibrios which differ widely from one another; sometimes several kinds are found in the same individual; at other times only one kind, in rare cases none at all. The animal experiment, so far as the reproduction of a true choleric lesion is concerned, has hitherto failed. In this group we may include also various other clinical forms of diarrhœa, which are undoubtedly due to infection, but the bacterial ætiology of which is as uncertain as that of cholera.

7. Lastly, there are a number of infective diseases, contagious it may be in the highest degree, in which no organisms have been separated, but which we presume to be due to bacteria. These are *syphilis, rabies,*

yellow fever, dengue, typhus fever, mumps, whooping-cough, small-pox, measles, scarlet fever, and *other so-called exanthemata.* Whether future research will prove them to be bacterial lesions it is hazardous to say; for the present they will be included under that heading, since the assumption of their bacterial origin constitutes a good enough working hypothesis, and one which at the same time can do no possible harm.

As there is variation in the morphology and chemical activity of bacteria, so there is also considerable *inconstancy in their activity in bacterial disease.* This hardly requires any further elucidation if we admit that the same micro-organism may vary in virulence, that it may produce highly toxic substances under certain conditions and bodies practically atoxic under others, that it may be readily attenuated, and conversely that its virulence and infective powers may be greatly increased. Change of chemical activity naturally implies change of activity in disease. Moreover, I have already pointed out that the same micro-organisms may be the cause of various morbid and pathological lesions. What this pathogenetic variability depends upon in all cases it is impossible to assert; sometimes, no doubt, on the resistance and insusceptibility of the individual, often on changes in the micro-organisms themselves, which we may guess at, but cannot define. Tuberculosis may appear in many forms, which clinically and pathologically are quite distinct; again the pyogenetic streptococcus may produce the most dissimilar lesions, and no less perplexing are the multiform activities of the pneumococcus. We shall deal later with personal insusceptibility. It is generally true that the better protected the individual the more likely is a bacterial infection in him to be followed by local reactive changes; and with regard to changes in the virulence of pathogenetic organisms, we find similarly that attenuated bacteria are capable of producing local changes only, while virulent ones are apt to be followed by severe general infection and disturbance. Enough has already been incidentally said on these matters in the previous pages, so that this short recapitulation must be considered sufficient. It is important to remember that amongst pathogenetic organisms in general, there is as little constancy of pathological potency as of morphological characters or chemical activity.

V. Infection and Contagion

A. Infection. — The term infection has frequently been used in the previous pages; now we shall fully consider its meaning. The use of the word is gradually becoming narrowed down to the signification which modern pathology and bacteriology have attached to it. A full discussion of older definitions is unnecessary; the time has come for uniformity of terminology. The connotation of a scientific term is liable to alteration, and it should be sufficiently plastic to adapt itself to new requirements. Infection as a clinical or pathological term dates from the days before the microbe was dreamt of as an important ætio-

logical factor of disease. Now that the veil has been lifted from the mysteries of bacterial disease, if we wish to keep the term, we must adapt it to modern ideas. Our ideas of infection and of intoxication are becoming more definite as bacteriological research advances. Formerly pathologists understood by infective diseases those which are set up by certain poisons, or poisonous substances (whether organised — that is living — or non-organised) either entering the body from without, or manufactured in and by the tissues of diseased individuals. They distinguished between a *contagium* and a *miasma*, the former being an endogenous virus developed in the diseased individual, while the latter was assumed to arise exogenously, that is, outside the diseased organism. According to this view contagious diseases can be transmitted only from man to man, or from animal to man, or conversely; while miasmatic diseases may be acquired by persons without coming into contact with individuals similarly affected. This distinction led to many difficulties. Anthrax, for instance, is always transmitted to man from an animal suffering from anthrax, yet it appears in animals without previous contact with similarly diseased animals; that is, the disease is contagious, in the older sense of the term, for man and miasmatic for animals.

With the advance of bacteriology the microbic nature of almost all infective diseases has been recognised, and we have gradually been compelled to modify our definitions. At the present time *we include under infective diseases only those which are caused by living pathogenetic germs which enter the tissues from without, and are capable of multiplying in the same.* A disease caused by substances not capable of reproduction, as, for example, gaseous or other chemical non-organised bodies, is an intoxicative process.

Though for practical as well as theoretical reasons we must distinguish between infective and intoxicative processes, we must remember that the chief lesions and symptoms following an infection are caused by the toxic products of the infection-carriers. This statement is true for almost all, if not for all infective diseases. In several infections we already have experimental proof of its truth (for example, in anthrax, diphtheria, tetanus, and suppurative infections). We may, then, pronounce the general law that *in any infective process due to a vegetable organism the chief lesions are due, not to the mechanical presence of the micro-organisms, but to the action of the metabolic products of these organisms.* Broadly speaking, we have an infection first and an intoxication afterwards; the latter, indeed, it is which gives the disease its specific and characteristic signs. The poison is manufactured within the body, and has not been introduced as such from without. The real difference then between infection and intoxication proper is that in the latter a poison is taken in as such, while in the former bacteria, introduced from without, prepare the poison or toxin in the tissues. In intoxication proper the effects are generally immediate; in an infective process an interval must elapse before a sufficient dose of poison has been produced. In the one case we have no incubation period, in the other we must have an incubation period of varying length.

Incubation. — The shorter this period the more the infective process resembles an intoxication. Some poisons produced by micro-organisms are harmful in comparatively large doses only, others will destroy life or give rise to symptoms in extremely small doses. Anthrax is a good instance of the more slowly acting poison; tetanus and diphtheria well illustrate the class of more active toxins. In tetanus we find that the bacilli multiply but slightly at the seat of inoculation; here, therefore, the mechanical effect produced by the presence of the bacilli may be entirely neglected. In infections such as anthrax, on the other hand, the bacilli multiply rapidly in the vessels; so that in mice, for instance, all the vessels of the body are, as it were, injected with pure cultures of anthrax bacilli, and the mechanical effect alone of the bacilli must be of some, if not of great importance. In diphtheria, also, and in septic embolisms the organisms may produce mechanical disturbances, directly or indirectly, which materially modify the symptoms caused by the toxins absorbed by the blood, lymph and tissues.

To sum up, then, *an infection leads to disease or death, either by intoxication alone, or by intoxication aided by mechanical interference caused by the presence of the bacilli themselves.*

The effect of such intoxication may be general or local. Examples of this we find in tetanus and diphtheria, or in rabies, where the poison causes general symptoms; while in other cases, as in certain forms of suppuration, the process remains localised. It is, however, extremely difficult to draw a hard and fast line between the two, as a local process may suddenly become general. I cannot dwell further on these points; the whole matter is extremely intricate, and premature generalisation must be carefully avoided.

The difference between infection and intoxication is well illustrated by certain kinds of food-poisoning. Firstly, there are cases where an individual, in perfect health, partakes of some article of food and dies a few hours later. The chemist succeeds in separating an alkaloidal poison, and animals fed with the tainted food die rapidly. Here we have a true intoxication. In other instances the bacteriologist separates a specific bacillus which, introduced by feeding into mice, produces in them illness and death after a definite incubation period, varying from twelve to twenty-four hours. At first sight both cases seem to be examples of food intoxication, for in each instance animals fed on the suspected food die. In the first case, however, death was directly due to a chemical poison introduced into the animal body as such; while in the other the disease did not set in until the second day after feeding, that is, not until the bacilli introduced had manufactured sufficient poison to bring about illness and death.

Infective diseases, then, are caused by organised beings, and an incubation period is characteristic of them.

B. Contagion and Contagiousness. — There is much confusion in the use of the terms contagion, contagium, contact, and contagiousness.

By *contagion* we understand what the German expresses by the word *Ansteckung; contagium* being the *Ansteckungsstoff;* while *contact* is equivalent to *Berührung*, and *contagiousness* to *Ansteckungskraft.* "Infective" and "contagious" are attributes which, partly through inaccuracy of expression, have been frequently confused, not only by laymen, but unfortunately also by serious writers who are not sufficiently careful about their terminology. Infection is the general term, and includes contagion. It stands to reason that a disease or lesion which is infective, as above defined, may be transmitted from the diseased to the healthy, since the germs which are responsible for the mischief are capable, it may be, of unlimited reproduction within the diseased body; but it does not necessarily follow that it is always, or even usually, thus transmitted. As instances, pneumonia, typhoid fever, and cholera may be mentioned; these are all infective diseases, but are they ordinarily contagious? Relapsing fever, again, is never transmitted from man to man; yet modern research has shown that when we transfuse the blood of a person suffering from it into the circulation of a healthy man or monkey, we may reproduce an attack in the new host. Under extraordinary, and generally artificial, conditions, therefore, even this disease may be contagious. [*Vide* art. on "Relapsing Fever."]

Contagion evidently may be either direct or indirect: that is, infection may be brought about either by contact directly from A to B, or indirectly from A to B through a third body C. For want of a better term, "contact" is here used in its widest, or at any rate in an extended sense, denoting not mere touch only, but also any form of infection or inoculation, whether through the broken or unbroken cuticle, the respiratory or alimentary tracts, or in any other possible way. We may distinguish therefore direct and indirect contact — diseases directly and indirectly contagious.

Whether a disease be directly or indirectly contagious, or both, will depend primarily on the nature of the organism which causes this disease. If an infective lesion be due to a strictly obligatory parasite, then it can be transmitted only by direct contact, that is, by immediate transference from living tissue to living tissue. The less parasitic, and therefore the more saprophytic the infective organisms, the greater will be the chances of transmitting the lesion by indirect contact; for in this case the organisms can thrive more or less well for a considerable time outside the animal body. This is a matter of some practical importance, because a disease which is exclusively directly contagious can be stamped out by isolation alone; while in a disease both directly and indirectly contagious isolation alone is of no avail; or, to express the matter in bacteriological terms, isolation can only prevent infective lesions due to obligatory parasites, and not lesions due to facultative saprophytes, or facultative parasites.

Arranging the more important infective diseases on this principle we find that there are —

i. *Diseases caused by strictly obligatory parasites* which readily perish outside the living animal body; these must be directly contagious, and

are best prevented by isolation, segregation, or destruction of the individual; assisted, of course, by disinfective measures. Examples are syphilis, rabies, gonorrhœa. The organisms, real or imaginary, which cause these diseases are of slight resistance, and soon die outside the animal body.

ii. *Diseases caused by obligatory parasites of greater resistance*, capable of surviving, for a little time at least, outside the animal body, although incapable of multiplying under such conditions; these, though generally or almost always directly contagious, may occasionally also be indirectly contagious. Examples are variola, scarlatina, measles, glanders, diphtheria. Isolation and segregation with disinfection are still the best means of preventing infection.

iii. *Diseases caused by facultative saprophytes*, or parasitic organisms capable of thriving outside the animal body; these are obviously either directly or indirectly contagious; and the greater the saprophytic faculty of the organisms, the greater the chances of indirect contagion. Segregation and isolation are utterly ineffectual as preventive measures; and absolute disinfection is theoretically the only means of prevention: in practice, however, this is almost always impossible. Examples are tuberculosis, actinomycosis, pyogenetic infections. It is quite possible that with increased knowledge of the biological conditions of pathogenetic organisms more than one disease at present included in the previous groups will eventually have to be placed in this one. Thus, as evidence accumulates, it seems more and more probable that the bacillus of diphtheria is a vigorous facultative saprophyte; and the same perhaps may in future be said of the pyogenetic streptococci.

iv. *Diseases caused by facultative parasites*, or saprophytic organisms capable of acting as parasites; these are hardly ever directly contagious, and occasionally not even indirectly contagious. Examples are anthrax, typhoid fever, cholera, tetanus. Anthrax is as a rule directly communicated from the diseased or dead animal to man (that is, directly contagious to man); the animal, on the other hand, generally acquires it, with its food, from fields or meadows where anthrax spores have been deposited from diseased animals (that is, indirectly contagious to animals): certain localities are breeding-places for the anthrax bacillus, and here an animal must acquire the disease independently of direct or indirect contagion.

The more widely these organisms are distributed the less contagious will be the diseases caused by them. Tetanus, for instance, is hardly ever directly or indirectly contagious; it is generally acquired independently of any previous case. During an epidemic of typhoid fever or cholera the respective organisms are generally so extensively diffused through water that contagion may practically be neglected.

Diseases caused by facultative parasites are frequently endemic in certain areas; thus cholera is constant in certain districts of India, in others it appears in epidemics. In the former case the organism must be pre-eminently saprophytic, and find the suitable conditions for growth in the soil or water. It stands to reason that isolation in such cases must be quite ineffectual, and that preventive measures must be directed

to the habitat of the organisms and against their further diffusion, whether by means of water-filtration, drainage, cultivation of the soil, or otherwise.

v. *Diseases which are infective but not contagious.*—Excluding malaria (which is due to plasmodial infection, and is not a bacterial disease), it seems that relapsing fever, due to a specific spirillum, is never transmitted by direct or indirect contact from one individual to another. It must be remarked, however, that our present knowledge of the bacterial pathology of this disease is very imperfect. These non-contagious blood diseases (relapsing fever and malaria) are always endemic, and can be avoided only by change of abode.

The Natural Mode of Propagation.—The public are always ready to assume, because a disease is due to organisms capable perhaps of unlimited growth in the body, and can be transmitted by inoculation from one guinea-pig or white mouse to another, that it is therefore always and under all conditions propagated directly from the affected individual to the healthy; which means that its diffusion depends exclusively on contagion. At once the cry is raised for segregation, separation and so forth, instead of pausing to study the natural mode of propagation of an infective disease. This evidently depends on many factors which may in part be deduced from the above statements:—

A. The germs never leave the animal body, or they do so in a state in which they are incapable of setting up a fresh infection. In this case there can be no contagion; the germs must have an abode somewhere outside the human body (relapsing fever is an example).

B. The germs as they leave the body retain full possession of their infective powers. If they retain both their vitality and virulence, then, and then only, can the disease be transmitted from the affected to the healthy; that is, it may be spread by contact, direct or indirect: but whether it is generally spread in this manner depends on the following points:—(α) The saprophytic or parasitic nature of the infective organisms, which has been sufficiently discussed above. (β) Their distribution and diffusion in space, or the readiness with which they either multiply or may be diffused after once leaving the animal body; if a germ be so widely distributed as to be almost ubiquitous, then we may practically neglect contagion as a means of spreading the disease (*v. supra*).

It is well to state here that aerial infection is less common than at one time it was supposed to be, and under ordinary conditions this mode of infection has been demonstrated only for pyogenetic, tubercular and pneumonic lesions; though it must be assumed to exist in influenza, (malaria), diphtheria, and some of the exanthemata, such as small-pox and scarlatina. For the organisms of typhoid fever, cholera, dysentery, and various forms of diarrhœa we must search the water; while the soil is commonly inhabited by the bacilli of tetanus and malignant œdema, and also of anthrax: pathogenetic pyococci are found likewise in the soil, which also absorbs the infective discharges of diseased individuals, discharges which contain organisms that, under favourable conditions, may survive for months. Dust may prove a fertile source of infection for

tuberculosis, wound infections, tetanus and pneumonia. That some bacterial diseases find their means of diffusion in food is so well known as to require no further comment. I may mention more especially tuberculosis, typhoid fever, cholera, diphtheria and scarlet fever. For the sake of brevity we must pass over the other possible sources of ectanthropic infections, such as insects, clothes, furniture and the like. Seeing, then, that the tubercle bacillus is found in the dust, in the food (milk), and in other accessible sources, we must pause before putting every fresh case of infection down to contagion, and before we recommend isolation of the diseased as the one preventive measure.

(γ) The power of the organisms to form spores outside the diseased body naturally lessens the importance of direct contagion and increases the chances of indirect contagion. (δ) The abundance of germs leaving the affected individual favours indirect contagion by causing a wider diffusion, and by offering more chances of ectanthropic infection. In some infective diseases the organisms are never, or but rarely, discharged from the body, as for instance in tetanus, where the bacilli are found in small numbers at the seat of inoculation; in others the organisms are discharged in large numbers, especially in the diseases which affect the excretory passages, or organs in direct or easy communication with such passages. In bacterial intestinal lesions, — for example, in typhoid fever and cholera — thousands of bacilli or vibrios must pass away with the dejecta: similarly in pulmonary infections — for example, in tuberculosis, pneumonia, influenza — the sputa must swarm with bacteria. From extensive ulcerating bacterial skin affections — as, for example, in nodular leprosy — myriads of bacilli may be discharged. (The breath, by the way, if unmixed with saliva or mucus, is free from micro-organisms.) The urine, again, may contain numerous organisms — as in gonorrhœa, some forms of puerperal fever, typhoid fever and tuberculosis. When the bacteria are incapable of saprophytic existence, or when from the nature of the disease the discharges can be more closely guarded, the danger of increased diffusion is so far limited. Thus the urine in gonorrhœa and the sputum in acute pneumonia are not dangerous sources of infection. On the other hand, consumptives by their expectorations contribute largely to the wide diffusion of the tubercle bacillus; from the chronic nature of their disease they are less easily controlled, and, especially in the poorer classes, they are reckless with their expectoration.

(ε) The mode and readiness of infection is naturally of great importance, for some organisms will produce disease in whatever way, and when they have been introduced into the body in very small numbers. Others are virulent when received in large numbers, or only when taken in by the stomach, and harmless when injected subcutaneously. Thus guinea-pigs succumb to the smallest injection of the tetanus bacillus, and white mice are so susceptible to anthrax that almost a single virulent spore or bacillus is sufficient to destroy them. Rabbits generally acquire a fatal septicæmia when injected with a very small number of virulent pneumococci. On the other hand, it requires a large

number of bacilli pyocyanei to bring about a fatal septicæmia in rodents, or a large number of pyogenetic staphylococci to produce suppuration. To some extent, no doubt, these laboratory observations apply also to natural conditions, especially since experiment shows that the result produced often varies as the quantity of germs introduced. Thus a small number of bacilli pyocyanei will lead to a small local abscess only, followed probably by a condition of acquired immunity; a larger number will lead to local necrosis, and a still larger number to septicæmia and death. The same direct relation between quantity and effect may be observed with many pathogenetic organisms. Koch found that white mice are resistant to tubercle bacilli inoculated subcutaneously, but succumb to subperitoneal inoculations, or when the bacilli are introduced by means of inhalation. The same rule applies also to dogs and rats: when large quantities of bacilli were used these animals failed to offer any resistance, whatever the mode of infection employed. Again, Blagovestchewski has demonstrated that, on simultaneously injecting the anthrax bacillus and the bacillus pyocyaneus into the anterior chamber or subcutaneous tissue of rabbits, no infection but on the contrary immunity against anthrax will result; while on injecting a similar mixture into the circulation the animal will die of a double infection. Roger, on the other hand, has shown that rabbits, which are naturally immune from quarter-evil, will succumb to this disease, if the bacilli be injected into the anterior chamber. It is evident, then, that *the easier and the more general the mode of the infection, both as regards the number of germs and the paths of infection, the greater the danger of spreading a contagious disease;* and before we estimate the true risk of contagion, we must find out what form of infection is necessary to produce the disease, what quantity of bacteria, and how readily such infection can be brought about.

(ζ) The natural habitat of the pathogenetic organisms greatly affects the ordinary risk of contagion. Thus the normal body on its cutaneous and mucous surfaces often contains large numbers of such organisms which may suddenly assume infective properties; that is to say, they may produce acute infection. In such cases contagion is a factor which may be neglected: a good example is pneumonia. (η) The contagiousness of an infective disease further depends on certain social, local, climatic and other hygienic conditions which cannot be discussed here. (θ) The susceptibility or predisposition of the individuals is a factor of far-reaching importance. When we test a microbe for its pathogenetic property, we always choose a highly susceptible animal — an animal, that is, which will acquire the disease under normal physiological conditions. When studying the contagiousness of any disease in man, we should recollect that the healthy body offers unequal resistances to the various germs and their poisons. Take, for instance, diphtheria or erysipelas, inoculate a healthy person with the morbid material, and diphtheria or erysipelas will result almost to a certainty. Do the same with leprosy or tuberculosis, and probably there will be no specific consequences.

Leprosy is not communicable from the diseased to the healthy and sound. The experimental evidence on this point is so strong that mere opinions to the contrary are of little importance. Many attempts have been made to inoculate leprosy from the leper to the non-leper, but never has a success been proved. Leprosy cannot be transmitted from the diseased to the healthy by means of inoculation — in other words, it is not contagious under normal conditions. To transmit the disease something else is wanted besides the *contagium vivum*, which is not sufficient of itself to produce leprosy; this something else may be a special predisposition, a want of resistance.

Contagion and contagiousness, then, cannot be measured by an absolute standard, a truth almost persistently forgotten. The scientific and the practical aspects of the question must be considered separately. In a scientific classification of infective diseases we justly include under contagious affections all those which may be propagated by contagion, that is by inoculation or any form of infection, irrespective of the fact whether they generally, or, indeed, ever are naturally spread in this manner. When practical sanitary and preventive measures are contemplated, the natural and epidemiological conditions must be carefully considered.

Summary. — Contagious infective diseases are spread by direct or indirect contact or — to put it in symbolic language — from A to B, so that B cannot be infected without A; or from A to B through an ectanthropic body X. In the first case, to save B we must remove or destroy A. In the second case three courses are open to us, namely, to find out whether we can best save B by destroying A alone, or X alone, or both A and X. But if we find that to destroy A alone is of no avail, and that to destroy X is an impossibility, what are we to do? Now, it is a well-ascertained fact that in many cases an individual has a natural resistance against the infective germ, and that the latter cannot exert its detrimental effect until this resistance is lost; and this may give us the key to action, which will be adapted to restore the resistance, while, at the same time, of course, X is kept in abeyance. To this point we shall return.

The micro-organisms responsible for a number of our commoner infective diseases belong to the group of facultative parasites, or facultative saprophytes, organisms which are capable of multiplying outside the human body. These diseases are seldom directly, and occasionally not even indirectly, contagious. A good example is cholera. The germs leaving the human body are, generally speaking, incapable of setting up an immediate infection. No doubt direct contagion does occur, but it is a rare exception; and sudden outbreaks of cholera are easily explained by assuming that large quantities of germs grow concealed and unsuspected outside the human organism, or that otherwise becoming diffused they have obtained access to a general source of infection, for instance the drinking water. The saprophytic nature or phase of the common bacillus, — if we assume it to be the contagium vivum of cholera — is of great importance

in regard to the contagiousness or non-contagiousness of cholera, and to the best mode of preventing further outbreaks or diffusion of the disease.

It has been said above that, if a germ be widely distributed in space, we may practically neglect contagion as a means of spreading the disease. This may be illustrated by the familiar instance of tuberculosis. Considering the large number of consumptives, the immense numbers of bacilli in the sputum, and the persistence of these bacilli, the sources of infection must be almost ubiquitous, and accordingly the exclusive importance of contagion vanishes. To go back to our symbols, we cannot remove X, or can do so in part only, because it is well known that the tubercle bacilli are capable of leaving the animal body and remaining dormant outside it for a long time, in the full possession of their infective and germinative properties. Dried they retain their virulence for months; boiling does not always destroy them, nor does putrefaction. The bacillus resists the digestive action of the gastro-intestinal secretions, and it is much less parasitic than is generally assumed. Thus, Sander has succeeded in growing it on ordinary potatoes and in their juice, on boiled macaroni, baked bread, and in ordinary tap water; and it is certain that it can be readily acclimatised to changes of temperature. Hence it is nearly certain that, within limits, it is capable of a saprophytic existence, and we are therefore forced to assume that, in towns at any rate, we are surrounded almost everywhere by infective tuberculous material. Infection, therefore, is possible in two ways, (*a*) from the diseased directly, or (*b*) from objects in the immediate vicinity of the affected person, or far removed both in time or space from him. To prevent further infection we should have to remove both the phthisical individuals and the bacilli scattered outside the human body. The former cannot be done satisfactorily, because phthisis is an extremely chronic affection, not always easily diagnosed in its early stages, and what is diagnosed as incipient phthisis is often a lesion considerably advanced. Isolation and segregation would therefore be followed by so little success as to seem unjustifiable. Nor can we entirely remove the ectanthropic sources of infection. We know, however, that only those of our fellow-creatures will acquire tuberculosis who are disposed to the disease; and the question is whether we can alter this disposition when once established, or altogether prevent its establishment? The answer will be supplied later.

We must understand that in reasoning upon laboratory experiments the precepts of logic and common-sense are not to be altogether forgotten. Laboratory experience, for instance, has taught us that tuberculosis is an infective lesion, due to a bacillus capable of multiplying within the body. It is also contagious; experiments on guinea-pigs prove this. But we must remember that guinea-pigs are extremely susceptible animals, and that the healthiest specimen, if inoculated with the smallest quantities of mammalian tubercle bacilli, will succumb. In the case of guinea-pigs segregation, destruction, and assiduous disinfection of the cages would keep the spread of tuberculosis in abeyance.

Mankind, on the other hand, is naturally resistant to tuberculosis.

This disease is directly or indirectly contagious for all healthy guinea-pigs alike; but in man it is contagious only for those who have lost their resistance, those, that is, who in some way or other have become disposed to the disease. In a well-regulated laboratory we prevent the outbreak, or at any rate the spread of phthisis among guinea-pigs by removing or destroying the diseased animals, and at the same time getting rid of the bacilli by disinfection. From our own surroundings, however, we can only remove the sources of infection in part; and so long as we cannot do so entirely, the destruction or isolation of the diseased subjects would be ineffectual.

The question of predisposition must now be studied more fully.

VI. Predisposition

I. Personal predisposition is best defined as susceptibility to a disease; it may be either natural or acquired. A natural predisposition may be either a property of a species, which as such is transmitted from parent to offspring (racial predisposition); or it may be an accidental character of one or more individuals of a species (individual predisposition), not necessarily transmitted to the offspring. Thus guinea-pigs are naturally extremely susceptible to tuberculosis; man to syphilis or diphtheria. On the other hand man or animal may be naturally resistant against an infective disease, as is a hen against tetanus. In the last case the resistance is absolute; that is, so long as we work within the limits of experiment, the normal animal cannot be infected; in other cases it may be relative and partial, as, for example, in the case of man's resistance against tuberculosis, leprosy, anthrax, or cholera. We must assume that in such cases the disposition is entirely or partly absent. The cause of this individual disposition we do not fully understand.

The predisposition, like immunity, depends on various factors, among which the most important are — (1) intrinsic cell properties; and (2) extrinsic conditions reacting harmfully on the body and its tissue processes. Within certain limits every organism has special cellular mechanisms to ward off an infection. Thus the acidity of the gastric juice, and a proper supply of it, may prove too strong for the cholera vibrio; the ciliated epithelium and the sensitiveness of the bronchial mucous membrane and the germicidal action of the mucus may protect the respiratory organs against an invasion by tubercle bacilli. Again, we know from Löffler's experiments that the age and nature of the epithelial lining are conditions of great importance in the case of diphtheria: the vaginal mucous membrane of young animals is easily attacked, but that of old animals is very resistant. Orth and Wyssokowitsch have shown that traumatic lesions at a seat of infection will cause a local predisposition to certain infective processes. These investigators produced a well-marked malignant endocarditis by first causing a slight injury to the cardiac valves, and then injecting a culture of staphylococci: endocarditis did not result when the valves were intact. Similarly pyogenetic

cocci will readily produce suppuration in an œdematous rabbit, although harmless to rabbits in a normal state.

The question of predisposition has been more clearly put before us during recent times, and a short summary may here be given of the most important experiments and observations which show that predisposition is a definite quality which can be estimated within the precincts of the laboratory, and is not a mere makeshift to explain clinical difficulties.

II. Acquired Predisposition.—Various means exist by which a refractory or resistant animal can be rendered susceptible—by which, that is, a disposition can be established to any particular infective disease; or, to put the case differently, we possess means to make a disease which is non-contagious to a certain species of animal extremely contagious to certain members of that species. We may reduce the natural resistance of an animal against a microbe either by general or special interferences, and thus establish an acquired disposition. The former are of more interest to us, as they prove how much good can be effected by sanitary surroundings in the prevention of disease, and we shall lead off with them.

General Interferences.—1. Canalis and Morpurgo have shown that by means of *starvation* we can render pigeons, which are naturally resistant against anthrax, extremely susceptible to this infection. They succumb, either if we allow them to starve immediately after the inoculation, or starve them six days previously and then inoculate them, at the same time continuing the process of starvation. But if we feed them regularly immediately after inoculation, then, in spite of having previously been starved for six days, they will survive. However, if we allow them to starve longer than six days before the inoculation, they will succumb, whether we feed them or not after the infection.

Similarly hens, naturally immune, become susceptible to an anthrax infection through starvation. White rats, on the other hand, do not lose their natural immunity in this manner. Sacchi, by means of starvation, succeeded in rendering a local anthrax infection in pigeons a general infection. Similar experiments have also been made on artificially immunised rabbits. Pernice and Alessi proved that dogs, hens, pigeons, and frogs can be rendered susceptible to anthrax, by depriving them of water.

2. Again, *fatigue and loss of blood* are capable of removing the natural immunity of animals. Thus Charrin and Roger have shown that the normal white rat, which, as is well known, is very insusceptible to anthrax, becomes susceptible to this disease in a marked degree, if it is made to work a treadmill in a cage until it is thoroughly fatigued. Roger has further demonstrated that rabbits, which are relatively refractory to quarter-evil, lose their immunity by exhaustion and fatigue; and Rodet and others have established an acquired disposition by inducing a general anæmia by artificial loss of blood.

3. *An unsuitable diet*, as Hankin has shown, may remove the resistance of the body against anthrax. Thus refractory rats, fed on sour milk and bread, lose their insusceptibility; a pure meat diet increases it. Hans Leo administered phloridzin in small doses with the food for some

days previous to inoculation, with the result that sugar showed itself in the tissues of the animal under experiment: this animal now became highly susceptible to a glanders infection, which in its normal condition it was able to resist. The same treatment, however, did not increase the susceptibility of rats to anthrax and tuberculosis.

4. *Exposure to heat, cold, and moisture* has been investigated by Pasteur, Petruschky, Fermi and Salsano, and others. Thus on immersing a hen in water it loses its resistance to anthrax, and the same occurs on reducing its temperature by the administration of antipyrin. Frogs, if kept at a temperature of 25°–35° C., will easily succumb to anthrax. Guinea-pigs and white mice, which are resistant to avian tuberculosis, can be rendered susceptible by keeping them after inoculation in a warm chamber at 33°–35° C. This will also increase the susceptibility of white mice to mammalian tuberculosis. Cold, on the other hand, does not affect the special disposition of these animals.

We see, then, that it is easy by such general means as starvation, fatigue, exposure, and bad diet to reduce the insusceptibility of certain animals to infective diseases. Now, if in a community of which the normal individuals are insusceptible, a certain number of these, through one or other of the above causes, become susceptible, then the disease may be extremely contagious for these modified persons, though non-contagious for the community as a group. This shows how cautious we must be in pronouncing any infective disease to be contagious to a community. In many cases it would evidently be absurd to clamour for physical or social extinction of the affected individual; we must attack the problem differently. Knowing by what processes the disease has become contagious for a certain community, while preventing a further distribution of the contagium by disinfection and other appropriate measures, we must so improve the social and personal hygiene as to reverse the direction of modification.

A consideration of tuberculosis from this point of view will make my meaning clearer. We cannot hope to destroy the *contagium vivum*, it is too widely distributed; nor can we destroy the affected individuals —such a process would be unavailing, even if free from other objections. How, then, can we prevent the spread of the disease? If, as it seems, the disposition to it be due to any or all of the above causes, let these be removed. Now we know that a healthy man is relatively immune from tuberculosis; we also know that bad hygiene, exposure, and the like, may render him susceptible to it; the rational preventive measure, therefore, is to counteract the causes of this acquired susceptibility, while at the same time we order all consumptives to destroy their sputum. That improved personal hygiene and public sanitation, and a higher standard of life materially diminish the death-rate from consumption is already ascertained; the vital statistics of England clearly demonstrate that sanitary legislation has coincided with a considerable diminution of the number of deaths from phthisis.

The same reasoning applies to leprosy. This affection, as mentioned above, is comparatively, if not quite, harmless to healthy men living under sound conditions. Bad hygiene, poverty, insufficient food, and so forth, increase the liability to the disease. How is it that the pest has died out in England and is decreasing in India? Certainly not merely on account of segregation, for such measures have virtually never been taken in Europe, and in India cannot be taken. In Norway the disease was decreasing before segregation was enforced. The chief cause of the disappearance of the leprosy from these parts is to be found in a general improvement of social and personal surroundings and a raised standard of living.

But why shall we not order the compulsory isolation of tubercular patients? Because in tuberculosis we have a chronic, extremely insidious disease, widely distributed over the world, a disposition to which is comparatively easily acquired or inherited; the tubercle bacilli already exist everywhere, and compulsory isolation could not be carried out rigorously enough to lessen the spread of the disease. Long before we have recognised the complaint, our patient, consciously or unconsciously, has already disseminated his share of bacilli ready to be taken up by the nearest individuals, and to fix upon the susceptible. If there is to be any isolation at all, the more reasonable course would be to isolate those so disposed. In the wealthier classes this is done, directly and indirectly, with good results. In the case of the masses the only thing to be done is to counteract the general causes of susceptibility, and to persist in disinfection on ordinary common-sense lines.

The above considerations will also explain the meaning and nature of *endemicity*, or the state, both of the individuals living in a district, and of the medium in which they live, which favours a certain infective disease. Undoubtedly cholera is a disease for which, if it appears sporadically, a special individual bent is required; and if it appears in epidemics, there must be the local predisposition in addition. Now in certain parts of India, as, for example, Lower Bengal and Assam, cholera is always present or "endemic." Such endemic areas are, for the most part, over-populated, poor, or extremely unhealthy. May not these and similar factors reduce the resistance of the population, and render the existence of the evil a necessary consequence? This matter gains in interest as we remember that in those areas wherein cholera is always present leprosy also is most common. This cannot mean that any direct causal connection exists between leprosy and cholera, but it is quite possible, and perhaps even probable, that those factors which contribute to the prevalence of the one have a like effect on the other.

We should, however, remember that, in contradistinction to this individual disposition which applies to certain individuals of a species, there is also a *racial disposition* which applies to all members of a species. Negroes are seldom affected by yellow fever, and the same is true of the mulatto. There are numerous examples of such phenomena in the laboratory. Thus of dogs which are relatively resistant to

anthrax, black dogs are less so than white ones. Black and gray rats are less susceptible to anthrax than white rats. Field-mice, again, are extremely susceptible to mammalian tuberculosis, while white mice are practically immune; white mice, on the other hand, easily succumb to an infection with the *micrococcus tetragonus*, while gray house-mice are quite refractory to it.

Again, age is a disposing factor, for young individuals acquire certain affections — for example, enteric fever — more easily than adults; this fact also is amply borne out by animal experiments. Oemler has shown that young pigeons are much less refractory to anthrax than old ones. But, strange to say, sucklings appear to be less liable to some infective fevers, such as measles and scarlet fever, than to others; this may be due to the protective influence of mothers' milk: this matter will be discussed later.

Here we must leave this interesting subject, and direct our attention to the effect on predisposition of certain more special and easily defined interferences. We shall find that apparently slight causes are capable of destroying the balance, and of removing with one stroke, as it were, the resistance, whether natural or acquired, of the tissues to a particular infection.

Special Interferences. — 1. It was once thought by Tizzoni and Cattani that it is impossible to render rabbits immune from tetanus after the *removal of their spleens*, and that the removal of the spleen will destroy the natural immunity of dogs from tetanus and anthrax. That, however, the acquired disposition does not in all cases depend on the removal of the spleen is shown by the experiments of Foà and Scabia and others, who worked with the diplococcus of pneumonia and the B. pyocyaneus, and proved that, for these infections at least and the immunity from them, the spleen is of no importance; for if we allow the animal to recover its weight and strength completely, its immunity will persist. The Italian authors, on repeating their experiments, have indeed come to this conclusion. The temporary loss of resistance is explained, therefore, simply by the shock and weakness which naturally follow the operation.

According to Canalis and Morpurgo, pigeons are rendered less resistant to anthrax by *removal of the pancreas*. This operation also predisposes animals to septic infections; and according to Sawtschenko, the same happens after section of the spinal cord in pigeons.

It is true, then, that the destruction or removal of certain organs may cancel the insusceptibility of an animal to an infection, either as a direct result of the ablation, or indirectly by the production of some constitutional change, such, for instance, as the diabetic which follows excision of the pancreas.

2. Again, there are many experiments to prove that bacteria, absolutely or relatively harmless to animals when injected in pure cultures by themselves, *become intensely virulent when at the same time we inject certain chemical bodies* at the seat of lesion. Thus Vaillard and Vincent have shown that in animals immune from tetanus a characteristic infec-

tion can be brought about by injecting lactic acid or trimethylamine with the tetanus bacillus. Similarly hydracetin and pyrogallol will destroy the acquired immunity of guinea-pigs against hog cholera. Bujwid found, on antecedent injection of sugar solution into the subcutaneous tissue of animals, that an inoculation of the staphylococcus pyogenes aureus was in most instances followed by marked suppuration; a result not easily achieved by means of the staphylococcus in the absence of previous sugar injection. Lastly, hypodermic injections of dextrose and lactic acid will render guinea-pigs and white mice susceptible to avian tuberculosis, and white mice also to mammalian tuberculosis. This was shown by Fermi and Salsano, and it is important to note that avian tubercle bacilli, repeatedly inoculated into guinea-pigs rendered susceptible by such injections, become virulent for normal guinea-pigs. Here we may also mention Klein and Coxwell's experiments, which show that in frogs and rats the natural immunity from anthrax may be destroyed by means of a chloroform-ether narcosis.

3. Then, again, the metabolic *products of certain, it may be harmless, micro-organisms are often capable of rendering a non-pathogenetic germ pathogenetic.* Examples of this are mentioned by Roger, who has shown that rabbits will succumb to quarter-evil, if, simultaneously with the bacilli, the chemical products of the bacillus prodigiosus, proteus vulgaris, or staphylococcus be administered. Klein and others have given further proof of this. Other allied bodies — vegetable ferments, for instance — have the same effect.

On the other hand, many of these chemical products of bacteria possess the power of destroying the pathogenetic property of specific organisms. I shall only refer to the experiments of Blagovestchewski, who showed that a simultaneous injection of anthrax bacilli and the products of the bacillus pyocyaneous prevents the lethal effect of the anthrax infection, and renders the animal immune.

4. What has been said of the chemical products of the bacteria applies with equal force to the bacteria themselves. Klein and others have shown that by means of *concurrent inoculations of various kinds of organisms* we may (1) render non-pathogenetic bacteria pathogenetic; or (2) increase or decrease the virulence of pathogenetic germs. A few examples must suffice: thus a simultaneous inoculation of anthrax and pyocyaneous bacilli, or of anthrax bacilli and erysipelas cocci, or of anthrax and prodigiosus or Friedländer's bacilli, protect the animal against the poisonous effects of the anthrax bacillus. On the other hand, the bacillus prodigiosus and various pyogenetic germs, if simultaneously administered with the bacillus of tetanus, render the latter extremely pathogenetic for animals capable of resisting a simple infection with the tetanus bacillus. Lastly, the virulence of the bacillus diphtheriæ is greatly enhanced by means of a concurrent inoculation of the bacillus pyocyaneus, as shown by Klein.

Summary. — We see, then, that the natural resistance of animals is easily destroyed by various processes: (1) by such as cause general

tissue disturbances, namely hunger, exposure to heat or cold and wet, fatigue, insufficient or inadequate feeding; and (2) by more special interferences, such as the removal of organs, essential or not to the animal economy, or (3) by concurrent inoculations with chemical or bacterial products, or with the bacteria themselves. These special interferences do not all act in the same manner on the animal organism; some — as, for example, the removal of glands — produce general changes in the body; but others may, and in many cases do cause a weakening of the tissues at the seat of inoculation whereby the local defensive processes are impaired and broken down; thus a foothold is given to the organisms, enabling them to grow and to manufacture their toxins. It must be confessed that our knowledge of the matter of concurrent inoculations or bacterial association and interaction is still defective. In the meantime these two processes (namely, the interferences which react on the whole body and those which react merely locally on the tissues at the seat of injury) must be considered apart as much as possible. In the latter case writers often speak of a local predisposition produced by tissue lesion; this is a misleading expression: it would be more correct to say that the predisposition has become evident after certain local changes. We cannot tell how far such local changes react on and disturb the whole body, although we must admit that in many cases it may not be a matter of breaking down an immunity at all, but merely one of soil — one of giving the organisms a chance of development by placing them under more suitable local conditions of implantation. The whole subject requires research rather than discussion; for the present it is enough to remember that, by means of association of bacterial or chemical substances with bacterial infections, we may either break down an existing immunity, or establish the existence of a latent predisposition, undetected, perhaps, because of the imperfections of our method of inoculation.

By any of the above methods, then — to express it differently — a non-contagious disease can at once be rendered highly contagious. The general causes are, in this connection, the more important, because they include conditions which are covered by the vague term "unsound hygiene." Before we can approach the question of the prevention of the spread of an infective disease, it is, therefore, our duty in all sanitary or other inquiries into its contagious nature to ascertain under what conditions it becomes contagious for a particular community. Contagionists, or those who believe in the direct contagiousness of all infective diseases, ask for some features and characters by which a disposition may be recognised. Such a question, while it discloses a want of appreciation of the difficulties of the inquiry, is also premature; our knowledge is not yet sufficiently advanced to enable us to define the special dispositions to given infective diseases. It is easy to scoff at vague generalities about unsound personal and social hygiene, but their potency in establishing a disposition to an infective disease is fully borne out by animal experiments; the precise application of this knowledge to a certain community can be made only on the historical and epidemiological experi-

ence, and the scientific evidence obtainable in the particular case. If it be found that the removal or abatement of unsound hygienic conditions is attended by a concomitant variation of the disease, we may be a step nearer to the proof of a correlation between those vague generalities about unsound hygiene on the one hand and contagion and susceptibility on the other. In many cases — as, for instance, in tuberculosis — we have to fight against these vague causes, for we believe that they render the disease a contagious one to a special class of individuals; and this method, together with personal disinfection, is the only possible way of dealing with the problem. That the removal or abatement of unfavourable hygienic conditions has undoubtedly brought about a decrease of phthisis, in England and in the large continental towns, is shown by recent statistics.

Certain writers, such as Baumgarten, deny the existence of a disposition to tuberculosis; our most experienced physicians and ablest pathologists, however, recognise its existence; until the days of bacteriology it had never been doubted. Flügge goes even so far as to say that "in tuberculosis we learn from experience that the greater or less accumulation of resistant infective agents plays a relatively subordinate part in the spread of the disease." (Flügge's *Micro-organisms*, translated by Watson Cheyne, page 752.) The physician counteracts the disposition by removing the susceptible individual from any possible risk of infection when sending him to warmer and sunnier climates; thus he isolates the predisposed whenever and so far as he can.

In conclusion, a few words must be said on *hereditary predisposition*.

Hereditary Predisposition. — Can an acquired disposition be transmitted from parent to offspring? Such a disposition may be called "hereditary," or "inherited," and must be carefully distinguished from a "congenital" disposition, which the child brings into the world independently of parental endowment. Tuberculosis is a disease of extra-uterine life, but undoubtedly cases of congenital tuberculosis do occur, as shown by Merkel, Landouzy, Rindfleisch, Birch-Hirschfeld and others; and much more frequently than congenital tuberculosis do we find tuberculosis in infants and children during the first months or years of life, as shown by Queyrat, Landouzy, Müller and others. Until recently it was almost universally believed that the undisputed hereditary succession of tubercular processes depends, not on a direct transmission of the elements of the disease from parent to offspring, but on an hereditary transmission of a proclivity. Baumgarten, however, believes that the heredity of phthisis depends on an intra-uterine or congenital infection of the fœtus with tubercle bacilli from the mother, and he supports these views with the following arguments. Besides the existence of congenital tuberculosis, Birch-Hirschfeld and others have demonstrated that in man, as well as in animals, tubercular infection through the placental circulation is not only possible but does actually occur. Observations and experiments on animals show: (*a*) that con-

genital tuberculosis in the larger susceptible mammals is not very rare (Johne); (*b*) that of the offspring of tubercular guinea-pigs twenty-five per cent are born with congenital tuberculosis (de Renzi); (*c*) that intra-uterine tubercular infection is possible in rabbits and mice (Gärtner); (*d*) that chickens hatched from eggs inoculated with tubercle bacilli manifest tuberculosis, and the eggs of canaries inoculated intra-abdominally with tubercle bacilli are frequently infected (Mafucci, Baumgarten and Gärtner). From analogy, therefore, Baumgarten assumes that in man also the tubercle bacilli are transmitted congenitally *in utero*, and that if the disease be not apparent at the time of birth the bacilli remain dormant in the tissues (of the liver for instance), causing at first only small obscure foci, and being for some time impaired in their development; but that eventually "through some cause or another" they awake and produce a manifest tuberculosis.

It is evident, if we accept Baumgarten's views, we have no longer any right to speak of "hereditary" phthisis; such a process as he assumes and describes is an infection from parent to ovum or fœtus, and is as much an infection as the transmission of pathogenetic organisms from one adult to another. We must then agree with Armauer Hanson that no specific infective disease is hereditary, if we use the term heredity in the sense which Darwin and modern biologists have given to it. If it appear congenitally it is simply communicated to the fœtus by infection. It would be absurd, for instance, to speak of an inherited gonorrhœal infection in cases in which newborn children are unfortunate enough to acquire a venereal ophthalmia in their passage into the world. Now, if heredity be not a factor in infection, the organisms must have been passed on: (*a*) from the ovary of the mother or the testes of the father; or (*b*) from the mother through the placental circulation; that is, infection may have been germinal or placental. Tubercles and tubercle bacilli have been found in the placenta, as already stated; and, further, there is sufficient evidence, anatomical and histological, to show that the bacilli pass from the placenta into the fœtal circulation. The evidence of germinal infection on the other hand is weak, so that it is safer to account for true congenital tuberculosis by placental infection.

But how are we to account for those cases in which the offspring of tuberculous parentage fall into tuberculosis years, often many years, after birth? Baumgarten assumes that in these cases also there is a latent infection, the tubercle bacilli having passed through the placenta (or from the ovum) into the fœtus, as already explained. That there may be an obscure tubercular process in many children of tuberculous parents must be acknowledged, because swollen and caseous glands containing virulent tubercle bacilli have been found both in man and animals at, or at any rate soon after, birth. Again, Mafucci working on animals often found tubercle bacilli in the liver of embryos of tuberculous parentage. Undoubtedly, then, tubercle bacilli may be stored up in the tissues of the fœtus. But how is it that such offspring often, or indeed generally, do not manifest the disease proper until years afterwards? The

answer must be because their tissues are sufficiently resistant to keep the activity of the bacilli in abeyance, or in some cases sufficiently strong even to destroy it altogether. But if later they lose this resistance, the bacilli are then placed in the conditions required for successful activity. A few bacilli in an obscure focus do not constitute tuberculosis any more than does the pathologist's tubercle or wart. We are thus led again to assume a proclivity in the cases under discussion. And is it not possible that the appearance of this proclivity is favoured by certain tendencies transmitted by inheritance? Hereditary peculiarities are often limited to a definite period or age; and we find that in the offspring the disease often shows itself at about the same age as it did in the parent — a fact of importance in a philosophical consideration of hereditary transmission.

Animal experiments cannot prove much in investigations of this nature, for in questions of hereditary transmission we must consider each species by itself. Guinea-pigs, rabbits, mice, hens, and canaries — the animals generally employed — are naturally highly susceptible to tuberculosis, and hence the predisposition is an inherent property of the parent, and therefore also of the ovum or embryo. As the tissues of the normal parent offer no resistance, we cannot possibly expect those of the offspring to do so. Baumgarten and his followers should have based their arguments and observations on animals of marked resistance — on goats and dogs — which cannot be infected without an artificially acquired disposition. Animal experiments do, however, make it certain that by no means all the offspring of tuberculous animals harbour latent bacilli in their tissues, and we have no right to assume that such a condition of things commonly exists in man. How then are we to explain the frequent occurrence of phthisis in the offspring of tuberculous parents? For the present we must assume that in most cases they inherit only the proclivity, and subsequently become infected from without. Hence the so-called "heredity" of phthisis finds its explanation in the following possibilities: — (1) Congenital infection, either germinal or placental, followed by immediate results; (2) Congenital infection with inherited disposition, followed, after a period of latency, by recrudescence at a subsequent date; (3) Inherited disposition with infection at a later date. Now since in the case of tuberculosis we find some of the characteristic features of heredity — for instance that atavism is not uncommon, and that the hereditary tendency is often limited to one sex and to a definite age — and since it requires great faith to believe in a bacterial sleep lasting through many years as a complete explanation, we must incline to Virchow's doctrine of the existence and influence of an inherited predisposition to tuberculosis, even though our modern conception of predisposition differs from his. [See article on the "Laws of Inheritance and Disease."]

The inherited disposition may be either specific or non-specific. The parental disposition may have been due to many agents and factors; and it is possible that some of these, although not of the same nature as the resulting tuberculosis, have been the cause of the congenital bent

transmitted to the offspring. This evidently could not be an inherited specific predisposition; that is, it is quite within the bounds of possibility that a non-tubercular condition of a parent may lead in a child to an inherited predisposition favourable to the development of tuberculosis. A predisposition can only be specifically inherited in cases in which the child was born of tuberculous parents or ancestors. A child born of a parent who becomes phthisical some years after its birth cannot with certainty be supposed to have inherited a specific tubercular proclivity. The eventual acquirement of the disease by the parent cannot make the inherited proclivity any more specific; it can prove only that certain conditions and abnormalities of the parent which eventually favoured tuberculosis have been transmitted to the offspring. For practical purposes the distinction between a specific and a non-specific inherited tendency may be unimportant; but in a scientific discussion of heredity it is a matter deserving of the fullest attention.

Germinal infection, though doubtful in tuberculosis, certainly exists in the case of syphilis; the contagium being derived either from the father or the mother. But since we have no direct knowledge of the syphilitic virus we cannot generalise from our observations of this disease. Although tubercle and also leprosy bacilli have been found occasionally in the testes and ovaries, and even in the seminal fluid of diseased individuals, there is no evidence whatever that germinal infection ever does occur: in fact Gärtner has shown that in animals, even if numerous tubercle bacilli are contained in the seminal fluid, it is the mother which is first infected, and not the ovum or embryo. This may be said of all infective diseases with the bacteriology of which we are acquainted; and for such of them as appear congenitally, infection must practically always take place through the placental circulation. This is exactly what occurs in animals where it can be demonstrated more readily. Placental infection in animals has been conclusively shown to occur in congenital anthrax, chicken cholera, suppurative lesions, and tuberculosis: in man it is found in pneumococcus and suppurative infections, in typhoid fever, anthrax (malaria), relapsing fever and tuberculosis; and is assumed to exist in measles, scarlatina, and small-pox, diseases the bacteriology of which is still obscure. Where placental infection occurs the micro-organisms are taken up chiefly by the fœtal liver; there, according to Mafucci, a keen struggle for supremacy occurs, the embryonic gland as much as the adult one being possessed of marked defensive capacity. If the bacteria prove victorious, then the fœtus may present the characteristic lesions produced by the infection — as for instance in many cases of tuberculosis, septicæmia, or pyæmia; or it may present them in a modified form, which after birth may assume the ordinary appearance, the embryo being, as already explained, apparently endowed in these cases with a more or less marked resistance. For instance, although anthrax bacilli, typhoid bacilli, and pneumococci may pass through the placental circulation, yet, as Dr. Welch says, "no instance has been observed in the fœtus of fully developed anthrax of croupous pneumonia, or of intestinal lesions by the

typhoid bacillus, although in several recorded instances these bacteria have unquestionably invaded the fœtus from the mother. The characteristic lesions have, however, been found so soon after birth as to indicate positively congenital infection." It is still a debated point whether the healthy placenta will allow pathogenetic organisms to pass into the fœtal circulation; some writers assume that a lesion such as a hæmorrhage, for instance, is necessary. It seems, however, that the factor is rather one of the time or duration of infection and of the virulence of the pathogenetic organisms. The lesson which we derive from these various experiments and observations on the fœtal infection is one on the use of the term heredity in respect of infective diseases; a strict terminology is, if possible, the more necessary now that Weissmann's hypotheses have so great an ascendency.

Immunity

Immunity is the converse of predisposition, and as we distinguish between a natural and an acquired predisposition, so must we distinguish between *a natural and an acquired immunity.* Again, as natural resistance may be racial or individual, so conferred immunity may be merely a temporary and personally acquired property, or it may be more permanent and transmissible from parent to offspring. All this follows from what has already been said of predisposition.

It is a difficult task in a few general words to give a clear and adequate account of the assumed nature and meaning of immunity, a subject which has been made the common fighting ground of pathologists, physiologists, biologists, and chemists, and which as yet we are far from understanding. Theory has succeeded theory; most of them have been but passing opinions, many have been based on the unfounded premises of incomplete research, a few bear the stamp of patient work and of careful observation. Most theories fail in their exclusiveness: the founder of a theory selects one phenomenon, which under given conditions occurs constantly, and makes it the corner-stone of his creed; but over his corner-stone he forgets the bricks. While attempting to peer into the mysteries of immunity, we must clearly remember how limited is our knowledge of the finer cellular processes, of tissue chemistry, and of vital reactions and reactivity. Again, our notions of infection, and of the process and mechanism of infection, are changing continually, as they become more extensive and move gradually from one field to another, touching now on chemistry, now on biology. Endless factors are concerned which require consideration and reconsideration; but of many of these factors, unfortunately, we know as yet but little.

Acquired immunity will most conveniently introduce us to the study before us. A susceptible animal may be rendered resistant against subsequent infection in different ways.

(*a*) *The natural proclivity to an infective disease may be removed in recovery from it.* This is Nature's way, and it has given us the key to the situation; individuals who have successfully struggled through an infec-

tion become more resistant against future attacks. In some cases this immunity is permanent, or at least of long duration; in others it is only temporary. Thus recovery from variola, typhoid fever, and the acute exanthemata, syphilis, yellow fever, mumps, and whooping-cough implies an immunity which lasts for years; while a successful stand against pneumonia and diphtheria leads but to a passing security. In some instances no immunity is apparent, or it is of extremely short duration, as in erysipelas, influenza, and cholera. In a general sense it seems to be the rule that recovery from an acquired infection is followed by increased resistance against the same. This principle was applied in the practice of variolation, which was revived and introduced into Great Britain by Lady Mary Wortley Montagu. The intentional inoculation with variolous matter was generally followed by a mild attack of small-pox which conferred on the individual a certain degree of immunity. The obvious objections to so dangerous a practice cannot be considered here.

(*b*) An artificial resistance may also be brought about by *inoculation with attenuated virus*, meaning by virus not the bacterial products, but the living micro-organisms or their spores. Vaccination, whether with humanised or calf lymph, is protection by means of inoculation with attenuated small-pox virus. There can no longer be any doubt that the variola poison becomes attenuated by transmission through calves or cows, and that the cow-pock is a modified form of variola vera. [See article on "Vaccination."] This method was established somewhat empirically, but in a strictly scientific manner, by Jenner. It was Pasteur, however, who recognised protection by means of attenuated virus as a principle. He immunised hens with weakened cultures of the B. choleræ gallinarum, as animals are made resistant against anthrax, quarter-evil, and swine fever, by inoculating them with attenuated cultures of the organisms of these diseases. Against these animal infections Pasteur's method of vaccination has proved a successful preventive measure. Although in the laboratory animals are easily rendered immune in this manner against the various bacterial lesions, and although this method of establishing an artificial resistance against fully virulent organisms by means of vaccination with less virulent organisms is one which has been widely used in experimental work, yet in medical as compared with veterinary practice the application of preventive vaccination has necessarily been limited. In fact, if we except Jenner's system of vaccination against variola, it must be said that the only disease against which attenuated inoculation has been tried — or rather is being tried — is Asiatic cholera. The principle of Haffkine's anticholeraic inoculations is practically the same as that first pursued by Pasteur. [See article on "Asiatic Cholera."]

(*c*) Instead of using attenuated cultures, *small doses of living and fully virulent organisms* may be employed to produce an artificial immunity. Thus 1 c.c. of a fresh broth culture of the B. pyocyaneus will without fail produce a fatal septicæmia in a rabbit; but if we inject 0·25 c.c. the animal, though it will certainly be ill, will show merely local changes,

and recover with an acquired immunity. To mention other examples would take us too far. In most cases the animal tissues can fight against minimal doses of bacteria, and perhaps there is no infective process which can be produced by a single unaided bacterial cell. It requires a certain minimum dose, which varies with the individual susceptibility, to produce a lethal effect; the body can resist the action of subminimal doses of living bacteria, so that we must assume that the tissues possess defensive or protective mechanisms, primitive and slight, perhaps, but capable of further development. Lubarsch has shown that mice and guinea-pigs, which are highly susceptible towards anthrax, may be fatally infected by a few bacilli, while the tissues of rabbits are capable of destroying hundreds of bacilli before their resistance, slight though it be, is overtaxed. There are, indeed, numerous instances of animals possessed of great natural resistance being liable to infection when inoculated with large or enormous doses of bacterial cultures. This explanation may not apply to all cases, but it is sufficiently established to justify the opinion that some of the factors of immunity — those, that is, which are concerned with the destruction of the bacteria — are vital tissue properties; in fact, that some of the germs of immunity are innate. The minimal lethal dose, of course, rises and falls with the virulence of the culture, and the virulence depends on the activity of the toxins, which is to great extent governed by the tissue susceptibilities; so that it is difficult for us from ever-changing premises to draw definite conclusions or laws. Judging from experiments, all we can say is that an animal is often able to resist living pathogenetic organisms, if injected in smaller doses. In all such cases the bacteria die, as mere saprophytes would do, in the living tissues, or lead to abortive lesions; while larger quantities — often only slightly larger — will readily bring about death, whether by means of a general septicæmia or of an intoxication or of a toxæmia. But our knowledge of all these processes is so limited that we must guard against an *ex uno omnes* argument; we must penetrate to the deeper relations of the facts, and must not be led away by superficial similarities.

(*d*) One of the most important discoveries in this field for research, one which has entirely altered our opinions regarding artificial immunity, is that of Salmon and Smith. Until their investigations were made, immunity was attempted exclusively by bacterial vaccination; these authors showed, however, that it is possible to protect against an infection by means of the inoculation, not only of the living bacteria, but also of their metabolic products or toxins, that is, by means of *chemical vaccination*. Salmon and Smith injected pigeons with the sterilised products of cultures of the hog cholera bacillus, and thereby rendered them resistant against subsequent infection with the bacillus itself. The matter was taken up by the various schools, and chemical or toxin vaccination soon became the most useful and accepted laboratory method for procuring artificial immunity; it is unnecessary, therefore, to give instances of the process.

Until this discovery was made immunity was supposed to depend on offensive or germicidal influences emanating from the tissues; but then it became evident that chemical processes must be concerned in the removal of a natural predisposition; that is, either during or after the act of protective vaccination, biochemical changes must occur in the tissues and their fluids, by which the body is rendered resistant against subsequent infection with virulent bacteria.

In most cases the toxins used are held in solution by the liquid culture medium, but it is quite immaterial in what form the metabolic products are given. They are equally potent in purer forms as albumoses, or peptones, or toxalbumins. Indeed, in many cases it suffices to inject the dead bodies of the bacteria — that is, the protoplasmic substances or proteins of their cells — in order to produce an immunity. *There is probably no essential difference between the processes of protection by means of toxin and protein vaccination.* We have some grounds for the assumption that the toxins which, as we have already seen, are most likely secreted by the bacterial cells, must at one time or another exist as such in the substance of the bacteria; so that, while injecting these so-called proteins, we inject the toxins. To this subject I shall return.

To render animals immune by means of chemical vaccination we generally use either attenuated toxins, or minute doses of the virulent poison; and gradually, by repeated inoculations, we accustom the animal to withstand larger doses: we aim, that is, at establishing a tolerance of the poison, or, as the German expresses it, at making the animal "*giftfest.*" The more potent the toxin the more cautiously must we proceed: impatience or haste may destroy the careful work of weeks or months. By often repeated administration of toxins, beginning with minute sublethal doses of fully virulent poisons or with larger doses of attenuated toxins, and gradually proceeding with increasing doses of highly virulent toxins, the degree of immunity may be greatly and even enormously raised. Or in like manner we may begin with attenuated bacteria, and gradually continue with increasing quantities of living virulent cultures. This method of continuous vaccination is the best means of obtaining the highest degrees of protection: the more toxin the animal absorbs the greater its immunity becomes. If for a time we give sublethal doses of bacterial toxins, the animal soon becomes resistant against the minimal lethal doses, and even against larger quantities, showing that the process of immunisation is "accumulative." Again, although at first we must proceed slowly and cautiously with subminimal doses, yet when the animal has been once rendered proof against the lethal dose, we may proceed more quickly. However, although in this manner we can produce extremely high degrees of immunity, there is a limit beyond which the acquired resistance cannot be raised. If we persevere with our injections, the animal may gradually lose its immunity again, waste, or die acutely.

Bouchard's Hypothesis. — Although we shall leave the theoretical discussion of immunity until we have reviewed, more or less in historical order, the various methods hitherto employed, it is well to discuss an im-

portant doctrine which is associated with Bouchard's name, although many other investigators have concerned themselves with it. Because it is possible to produce immunity by means of bacteria deprived of their toxins or rendered atoxic by means of attenuation, Bouchard and Hüppe assumed that the bacteria secrete protecting substances besides their deadly toxins, and that these protective substances — which either enter into solution if the organisms are grown in liquid media or are retained in the bacterial cells, and must not be confounded with the bacterial proteins — when incorporated by the tissues bring about the immunity; so that the immunity conferring substances and the toxic bodies, though both the products of bacterial activity, are essentially distinct. The fact that the highest degree of immunity is produced by employing the most virulent toxins or cultures in the largest possible dose reduces this notion to an absurdity. We are capable of protecting animals against snake venom or tetanus by means of continued injections of the respective poisons, beginning with minute doses and slowly passing on to large doses, till eventually we render them intensely immune. Since, up to a certain limit, the resistance produced varies with the amount of poison injected, we cannot logically believe that the toxic substances injected into the tissues are combined with an immunising substance from the beginning, but we must suppose that the changes in the animal organism which result in immunity are produced by the toxins. Without the use of highly virulent cultures or of toxins of great activity it is impossible to obtain a high degree of immunity.

Another point of importance, especially for subsequent theoretical considerations, is the fact that after successful protection the animal is capable of resisting both the toxin and the living culture. *By means of chemical or toxin vaccination it becomes refractory to subsequent inoculation with living cultures, that is, to a bacterial infection; and by means of bacterial vaccination it becomes refractory to subsequent inoculation with the toxins, that is, to bacterial intoxication.* Though it is easy to protect an animal by means of toxin against the bacteria producing that toxin, we frequently observe that it will successfully resist the bacterial infection at a time when it is still very sensitive to the toxin itself. But if we persevere it will in time become tolerant of the poison as well. Metschnikoff at one time thought that an animal vaccinated against a bacterial culture is not necessarily proof against the poison produced by that culture. He quotes experiments performed by others, showing that by chemical vaccination we may confer upon rabbits, in a few days, an immunity from certain infections (vibrio Metschnikovii, B. pyocyaneus, bacillus of hog cholera, pneumococcus) yet the animals remain as sensitive towards the toxins of these organisms as if they had not been vaccinated at all. These observations, however, are based on insufficient experiment; for if we only continue long enough with the inoculation of toxin we invariably succeed in rendering the animal proof against intoxication. Of course we could not expect an animal treated with small doses of poison at once to become refractory to large doses of the poison; there are proportions in all things. But we do find — for instance, in the case of cobra poison — that after a comparatively

short course of a 0·25 milligramme dose, the animal will successfully resist a whole milligramme: it is simply a question of time and patience. The same is true of all bacterial toxins whether we use tetano-toxin, diphtheria toxin, or other poisons; if the animal has been properly treated with gradually increasing doses of a toxin, it becomes proof against both infection and intoxication. *Immunity, therefore, implies resistance against the bacteria and their products.* The importance of this law, for such it is, we shall grasp more fully presently when we come to discuss the theoretical aspects of the subject.

(*e*) The experimental study of immunity gradually disclosed remarkable properties of the animal serum and the tissue fluids, the recognition of which formed the foundation of methods of protection and treatment adopted at the present time. Fodor showed in 1887 that the fluids of the normal living body, and especially blood, are germicidal, are capable, that is, of destroying bacterial life. Buchner, Behring, Nuttall and Nissen extended Fodor's observations, and it was soon learned that the antimicrobic influences of blood exist also in the serum, and moreover that the capacities of various animals are very diverse; that is to say, the blood or serum of the various species of animals is not equally destructive to all bacterial forms alike: in some animals it either has no such power, or it is harmful only to certain micro-organisms, and harmless to others. The final outcome of these observations we find in one of the greatest triumphs of preventive medicine since Pasteur's earlier discovery, in the prevention and cure of infective and intoxicative lesions by means of the injection of serum derived from protected animals. Behring step by step built up the law, that *if an animal has been artificially protected against a particular infective agent, its blood or serum acquires the power, when injected in sufficient quantity into another animal, of directly transmitting an immunity from that agent.*

Experimentally this law is so firmly established, that it is now one of the articles of bacteriological faith. A few examples may be mentioned: —

(1) Having succeeded in the artificial protection of rabbits and other animals against tetanus, Behring and Kitasato (1890) by injecting highly susceptible white mice with serum derived from the protected animals, rendered them insusceptible to tetanic infection and intoxication.

(2) Similarly Behring and Wernicke (1890 and 1891) demonstrated that the blood serum of animals artificially vaccinated against diphtheria has the power of protecting susceptible animals against an infection with the diphtheria bacillus, or against an intoxication with the diphtheria toxin.

(3) Babes and Lepp had already (1889) shown by experiments that the blood of dogs vaccinated against rabies, when injected into susceptible animals, confers a certain amount of protection against subsequent inoculation, and concluded from their observations that the possibility of vaccinating with the fluids and cells of animals which have been rendered refractory to the disease must be admitted.

(4) Ehrlich (1891) clearly brought forward the important fact that Behring's law applies not only to bacterial intoxication, but also to intoxications with other organic toxins. He succeeded in establishing in mice a marked tolerance of ricin (obtained from castor oil beans), and of abrin (obtained from jequerity seeds), by administering gradually increasing doses either under the skin or by the mouth; and he found that the serum of ricin-proof animals possesses the power of directly transmitting a resistance against ricin, and that the serum of abrin-proof animals is capable of producing the same effect with regard to abrin. These observations are of far-reaching importance, because they open up a wider field for the application of Behring's method; and, as we shall see later, they emphasised, from the theoretical point of view, the conflicting opinions on immunity which at that time were stoutly defended.

It would take us too far to enumerate all the various bacterial infections on which Behring's law has been tested in the laboratory. To give a convincing proof, however, to those who may be still in doubt, it may be stated that the protective power of serum obtained from animals rendered immune from the effects of bacterial inoculations has been demonstrated for infections with mouse septicæmia, Friedländer's pneumonia bacillus, Fränkel's pneumococcus, the typhoid bacillus, the vibrios of Asiatic cholera, B. pyocyaneus, streptococci and staphylococci pyogenes, B. prodigiosus, and the B. coli communis. The extensive experiments of Calmette, recently confirmed by Professor Fraser, prove that a protective serum may also be obtained from animals gradually rendered proof against various kinds of animal poisons such as snake venoms, physiologically and chemically closely allied to bacterial toxins. If we arrange these facts systematically, we shall find that the lesions for which serum protection has been tried are very diverse. They include—

(i.) Bacterial infections which are pre-eminently intoxicative, such as tetanus and diphtheria, in which the bacilli, in larger or smaller numbers, are found only, or chiefly, at the seat of infection, where they produce their deadly toxins.

(ii.) Bacterial infections in which the organisms spread widely into the tissues from the seat of inoculation, either along the lymph channels or by means of the circulation (hæmic infections).

(iii.) Direct intoxications with the poisons manufactured by the bacteria, intoxications with other animal or vegetable poisons belonging to the group of so-called toxalbumins, and lastly, intoxications produced by substances the real nature of which is still unknown, for example, rabies.

The protective serum is, therefore, in some cases active against the bacteria themselves; in others against their products, and in yet others equally powerful against the effects of the living organisms and of their toxins. No doubt the pathogenetic bacteria call forth the lesions and general symptoms of the disease which they produce by means of their poisonous activity; so that, although the obvious pathological phenomena considered generally appear extremely heterogeneous, yet the common principle of intoxication underlies them all. It would almost seem

that the stronger the toxic faculty of a particular organism, the less disposed is the latter to invade the tissues and the blood. This much is certain that an animal, whether vaccinated with the living bacteria or with their metabolic products, will, when once protected, give a serum which is essentially, though perhaps not indifferently, active both against a subsequent infection with the living organisms and against a subsequent intoxication with the toxins. Since the poisonous products are the chief weapons of infection, we must regard the action of the protective serum as directed especially against the effect of the poison; hence this serum has been called "antitoxin," an ill-chosen name.

It was further shown by Behring and his pupils, that the protective serum can exert its marvellous power even *after a preceding infection* — when the symptoms of disease or intoxication have already appeared; *the protective serum is therefore also curative.* It is obvious that to bring about a cure must require larger quantities of serum than are necessary for protection; moreover, the chances of a cure vary directly with the promptness of administration. That protective serum is also curative is firmly established, so far as experiment goes, for all the various processes mentioned above, including intoxications with vegetable and animal toxalbumins.

There is a striking difference between immunity produced by the inoculation of the bacteria themselves and their toxins — whether attenuated or not, and immunity produced by serum injections. In the former case the animal gains its immunity after an active struggle with the disease or lesions following the injection or intoxication; in the latter case there is no struggle with disease, and no reaction; the animal remains passive, while the immunity-conferring substances are applied to its tissues. On account of this essential difference, Ehrlich distinguished active and passive immunity. Passive immunity is effected quickly, is less persistent, and varies with the amount of serum used and with the degree of immunity of the animal which supplies the serum. Active immunity, on the other hand, does not appear for days, not until the animal has passed through the reactive stage; then it becomes permanent, and is proportional to the intensity of the reaction rather than to the amount of vaccine used.

(*f*) Within recent years it has also been shown that an artificial *immunity may be produced in animals by feeding them either with the living organisms or their products.* Ehrlich and Fraser have applied this method in the case of the vegetable toxins (abrin and ricin) and the snake venoms. An animal can be protected also against tetanus, diphtheria, cholera, and other infections in this manner; and what is more, the serum obtained from them has acquired preventive and curative powers.

Although other methods of producing artificial immunity in animals have been described, it is more convenient to defer the consideration of them; because these six processes, briefly described, form a progressive series which much facilitates the theoretical discussion. To this discussion we shall now pass on.

Theory of Acquired Immunity. — A number of hypotheses have been

built up to explain the processes in the animal body by which the immunity is gradually developed. Many of these have been but ingenious speculations, based often upon a single process observed, it may be, with brilliant genius and acuity. It must be remembered that a theory can take no other foundation than the observation and experience of conditions recognised or recognisable at the time; nor can it be tested in advance of contemporary knowledge. Retrospectively we now discard many theories, the discussion of which in the period of their ascendency led to much heated controversy; for in the light of new discoveries they are seen to be incorrect or insufficient. Many theories fail because they attempt to explain a process by selecting a particular factor as the cause, instead of recognising in it what it actually is, a concomitant variation. As I have given the methods of producing artificial immunity more or less in historic order, it will be well to consider the theories of acquired immunity in the same manner.

(*a*) *Pasteur's hypothesis of exhaustion*, which was shared by Klebs, assumed that the attenuated micro-organisms, which were injected into the animal tissues for the purpose of establishing a protection, used up and thus removed from the body certain substances of vital necessity for the bacteria in question; and that the animal body once deprived of these substances remained permanently exhausted, so that if bacteria of the same kind subsequently obtain access to the tissues they find no suitable soil for further development. This hypothesis was deduced from test-tube observations; for evidently a given amount of nutrient matter can only offer nourishment to a certain quantity of micro-organisms, and when the soil is exhausted growth must cease.

(*β*) This hypothesis was doomed to fall, as soon as it became known that artificial immunity is better produced by the administration — subcutaneous, intravenous, or gastric — not of the bacteria, but of their metabolic products, substances which possess no life and cannot, therefore, use up tissue materials. Starting from other observations on the growth of bacteria in artificial media, Chauveau and others had already preached the theory of *retention*; according to this theory the bacteria not merely deprive the body of material necessary to their growth, but also leave products behind which are absorbed, accumulated, and retained. The retention of these substances was supposed to make the tissues unsuitable for subsequent infection. This hypothesis was apparently supported by the facts of protection by means of chemical vaccination, — that is, protection with bacterial toxin, — but it is also a test-tube argument; for we know that many organisms, especially those which produce active fermentations, either by primary secretion or secondary fermentation, manufacture substances which are deleterious to their own further growth and activity. The yeast cells, for instance, by forming alcohol compass their own death and destruction.

Although the retention hypothesis is much nearer the truth than Pasteur's cruder notion, there are serious objections to it which compel us to abandon it, and these are —

(i.) The artificial immunity is frequently of long duration, and we cannot possibly assume that such a permanent change from susceptibility to insusceptibility could be due to the absorption and retention of soluble toxins, which, so far as we know, are not retained by the body, but, as clinical and pathological observations prove, are readily eliminated. In many cases the specific toxins can easily be traced in the urine during the development of immunity by chemical vaccination.

(ii.) In most, or in almost all cases, the blood, serum, or tissue juices of animals artificially protected by the administration of bacterial poisons, form good culture media for the micro-organisms concerned. We shall discuss this point more fully hereafter.

(iii.) An artificial immunity, as shown above, may be readily broken down by interferences which can hardly affect the retention of the metabolic bacterial products. There can be no doubt that the stability of an acquired immunity must be due to reactive virtues acquired by the tissues and the cells themselves, and not to something left behind by the micro-organisms.

(iv.) Immunity may be produced by the injection of micro-organisms which have become so attenuated as to be little more than mere saprophytes.

(γ) It is the merit of Metschnikoff to have searched for a cellular theory of immunity, and to have formulated *the theory of phagocytosis.* This has already been fully considered in the article on Inflammation, where all the important phenomena of phagocytosis are described; the matter need not, therefore, be re-opened here. Metschnikoff, who it must be remembered built up his theory at a time when chemical vaccination with bacterial products was unknown, assumed that by means of inoculation of attenuated micro-organisms the leucocytes and phagocytes, incapable at first of fighting against bacteria possessed of their full virulence, gradually acquire, by adaptation and selection of the fittest, the power of ingesting and destroying even these. If such acquired cell properties be transmitted from cell generation to cell generation, the animal body becomes protected against future invasions.

With the discovery of chemical vaccination and serum protection, Metschnikoff, reluctant to abandon his theory, had to modify his views continually. He assumed that the injection of soluble toxic or protective substances into the body has an "educational effect" on the phagocytes, by which they are taught to overcome bacteria which previously were invincible. Undoubtedly phagocytosis exists, and is perhaps one of the commonest phenomena of immunity; but it is not permissible to speak, as Metschnikoff does, of an "education of leucocytes to attack and destroy bacteria"; let us substitute the real word, and it reads "acquired immunity of leucocytes enabling them to remove the bacteria which come in their way." If we do this, then we find that we are little farther than before; we have merely thrown the mystery a step farther back, that is, from the body as a whole to a small cellular portion of it, the phagocytes. Immunity of the body would depend on immunity of the leucocytes and

their conversion into phagocytes. But how do the leucocytes acquire immunity? Metschnikoff says they are "educated" to attack, "educated" to conquer; obviously this is no explanation. Furthermore, no pathologist who views the animal body as a complex structure, and not merely as a congeries of amœbæ, and who appreciates the adaptation of the tissues to diseased conditions, — as illustrated, for instance, by the phenomena of compensation, — can assume that immunity, a general process, is brought about by one specified set of cells. Metschnikoff's observations are extremely beautiful and almost dramatic; we admire his zeal and penetration; but the advances of recent years, apart from any other considerations, compel us to give up his theory unconditionally. As soon as we realise that the symptoms of infective lesions depend in the first instance on the bacterial toxins, and that acquired immunity implies protection against the poisons as well as against the bacteria, it becomes evident that no theory of artificial immunity can be correct unless it explains both processes. Phagocytosis cannot do this, hence it was doomed as an exclusive theory to fall. So long as the bacterial poison is not neutralised or destroyed in the body, it matters not whether the bacteria are eventually killed or not. An animal made immune from a living microbe can also resist the toxin of such microbe to varying degrees, and, conversely, an animal rendered proof against the toxin will also resist the living microbe. Immunity from the toxic effects cannot be explained by means of phagocytosis. The proof that the animal body possesses other defensive means quite independent of phagocytosis has contributed greatly to the decline and fall of this attractive and once dominant theory.

(δ) This proof was first demonstrated by Grohmann in 1884 and by Fodor in 1887, who clearly showed that *the normal tissue fluids, and more especially the blood, possess marked antimicrobic properties.* These earlier observations were followed up, especially by Nuttall, Behring, and Buchner, who established further that the offensive action of the blood has its source in the albuminous bodies of the cell-free serum, which no doubt are primarily derived from the cells, wandering or fixed, phagocytic or non-ingestive. Buchner and Hankin took the lead in explaining this action, and suggested that the destructive power of serum is due to certain proteid substances to which, unfortunately, he gave the name of *alexins.* It must not be assumed, however, that the blood of any animal has a general antimicrobic action, or even any at all. In some cases it is quite powerless, and, moreover, its potency frequently varies in different members of the same species. As these observations, however, relate to natural rather than acquired immunity, their discussion must be deferred for a while. Here I shall make an attempt to explain, if this be possible, the law discovered by Behring, that an animal whose resistance to a bacterial disease has been considerably increased, possesses a blood capable of neutralising an infection or intoxication of the same bacterial origin.

(ε) It was shown by Behring and others that, speaking generally, *the blood serum of naturally immune animals does not possess any or but slight antimicrobic, antitoxic, or protective properties.* Thus, for instance, the

serum of a hen, which is naturally refractory to tetanus, cannot protect other animals, nor can it "neutralise" the tetanus poison. There are instances, it is true, where the serum of naturally immune animals possesses a germicidal power; rat's serum, for example, will destroy anthrax bacilli, but that of mice, guinea-pigs, rabbits, sheep and cattle, all naturally susceptible animals, is without effect. There are a few cases of such correlation between natural immunity and the antimicrobic power of the blood, but they must be regarded as exceptions; we cannot explain a specifically acquired immunity by merely assuming that an increase of a natural pre-existing germicidal power has taken place; it must be due to acquired and superadded changes. The best corroboration of this opinion is the fact that if tetanus bacilli or their toxin be injected into the refractory hen, its serum is thereby rendered active against tetanus. Hence, in the first place, it is necessary that even in refractory animals reactive changes should be produced before their serum becomes in any way protective for others. The tissue cells, therefore, are primarily brought into conflict with the bacteria and their products, and, if they conquer, it is by virtue of antagonistic substances, which are produced by them partly anew, partly out of existing elements, are absorbed or dissolved by the body fluids, and are thus distributed through the animal organism. By renewing the struggle from time to time we can raise the power of these antagonistic substances; and the keener the battle, that is, *the more susceptible the animal was, the stronger this power will be.* Further, *the action of the protective serum is specific, that is,* the serum of an animal rendered immune from a particular infection will with certainty protect other animals against this infection only. Although this assertion must be accepted with certain reservations, at present the evidence against it, as a general principle, so far as bacterial infections or intoxications are concerned, is not strong enough to raise grave doubt or to invite discussion here. There are numerous varieties of cholera vibrios which apparently are closely allied; yet an animal rendered immune by specific inoculation from the infection of one of these will produce a serum active against this variety, powerless against others. Again, closely as the pathological effects produced by the streptococci and staphylococci resemble each other, yet an anti-streptococcus serum is useless against the staphylococci. And yet again, although by means of intra-peritoneal injections of the B. prodigiosus it is possible to protect rabbits against intra-peritoneal injections of the B. pyocyaneus, nevertheless the serum of an animal protected against the B. prodigiosus cannot render another animal immune with regard to the B. pyocyaneus, although the serum of animals protected simultaneously against both the B. prodigiosus and the B. pyocyaneus will protect against both infections. We shall come back to this argument.

How does the protective serum act? Does it act (1) as an antidote to the toxins, or (2) as lethal to the bacteria? If we mix in a test-tube a certain quantity of diphtheria or tetanus toxin with the necessary amount of the corresponding serum, the mixture injected into an animal is harm-

less, the poison appears to be neutralised. Recent observations by Buchner and others seem, however, to contradict this assumption, seductive as it is on account of its simplicity. A neutralisation, as Behring pictured it to his mind, comparable to that combination of an acid with an alkali, which, by means of chemical or physiological interaction, leads to a neutral compound, can hardly be the explanation of the marvellous phenomena, because it has been found that the apparently neutralised mixture, though harmless for less susceptible animals, possesses a highly toxic action on more susceptible animals or on weakened individuals of the same species. Thus Buchner has demonstrated that a mixture of tetanotoxin with tetanus serum, in the exact proportion which renders it impotent for mice, is still toxic for guinea-pigs which are much more susceptible than the smaller rodents; and Roux and Vaillard have shown that a mixture of diphtheria toxin and antitoxin, harmless for vigorous guinea-pigs, will kill weakened individuals. We cannot then assume that the poison has been permanently destroyed by the serum. It has, therefore, been thought that the protective bodies do not directly attack the toxins, but act by producing a resistance of the tissues so rapidly that on injecting the toxin together with the antagonistic serum we have, so to speak, a race between immunity and intoxication. Objections may be raised to this view also, and with our imperfect knowledge we cannot give a casting vote for one theory or the other. Fränkel assumes, so far as the antitoxic power of the protective serum is concerned, that the toxin and the antagonistic substances (generally called antitoxins), though they do not neutralise one another so as to form a harmless stable compound, enter nevertheless into a looser combination which results in a temporary suspension of the poisonous activity of the toxic constituent; a combination which may, however, under special conditions be split, and the toxic constituent once more become free. We have as yet no proof in favour of such an hypothesis. Moreover, we must not forget that there is no absolute standard of virulence or toxic effect, that the toxic coefficient must naturally vary for each animal; thus in estimating whether a poison has been really rendered inocuous we must use the most susceptible animals. We shall then find that a toxin to which serum has been added so as to neutralise it for such animals will be harmless for all others. A more or less refractory animal is, from its very nature, able to account for a greater or less fraction of the poison, so that the protective serum is only called upon to neutralise the surplus. This may explain Buchner's difficulty, that a mixture of tetanus toxin and anti-tetanic serum, though harmless to the more refractory mouse, is still harmful to the more susceptible guinea-pig. At present it seems more reasonable to accept the antitoxic or neutralising power of the protective serum — not indeed as an ordinary test-tube reaction, but rather as a vital cellular change. Yet since the toxic value is a relative quantity varying with each species of animals, the antitoxic value must also be a relative quantity.

In the next place we must ask (2) whether this serum possesses any destructive action on the bacteria themselves; is it antimicrobic? Though formerly it was assumed to act as a direct poison to the bacteria, after

the manner of a disinfectant; or to contain substances which, when in contact with the tissues and their juices, render these destructive to microbic life; yet it was soon recognised that acquired immunity cannot be explained by the germicidal effect of the serum itself, or by a germicidal quality induced in the animal body.

Experiments show that anti-diphtheritic and anti-tetanic serum form by no means unfavourable culture media for the respective bacilli, though it is certain that on administering these protective fluids together with the organisms, the latter are arrested in their growth or eventually even destroyed. Earlier observations made it appear that the serum of a protected animal is distinctly germicidal; thus, although the vibrio of Metschnikoff, for instance, thrives well in a serum obtained from a normal guinea-pig, when this animal has been rendered immune its serum will no longer allow the vibrios to flourish. But as in the case of natural immunity, it is quite the exception to find a germicidal serum, so we find also that the serum obtained from a protected animal seldom has this property. So far as the direct destructive power of protective serum, measured by test-tube reactions and phenomena, is concerned, we find so little correlation between artificial immunity and bacterial destruction, that we cannot look for an explanation of acquired immunity in a change of the serum from a nutritive to a destructive one. Yet we find that in the animal body the protective serum will prevent lesions essentially infective, such lesions, for example, as a septicæmia dependent on a general overgrowth and diffusion of the bacteria throughout the tissues.

Bouchard and his school assumed that the process of protection alters the serum in such a manner as to render it attenuating; so that although it may be unable to destroy bacterial life, it nevertheless becomes capable of altering the chemical and toxic activity of the organism concerned to such an extent that it ceases to be virulent. Thus anthrax bacilli grown in the serum or blood of vaccinated sheep apparently lose their virulence; so do erysipelas cocci cultivated in serum of protected animals; and the same rule applies to the pneumococcus and B. pyocyaneus. Although these observations directly refute the theory which assumes that artificial protections lead to the formation of germicidal substances in the blood, they would seem to show that these processes endow the tissue fluids with a marked attenuating power, so that deadly organisms grown in them become capable of producing more than a passing and insignificant lesion. Metschnikoff, however, has conclusively demonstrated the incorrectness of this supposition. Firstly, this attenuating effect is not a constant result of acquired immunity; secondly, it is merely apparent and very transitory, while true attenuation is a more lasting change; thirdly, if we separate the bacteria from the serum in which they grow by means of filtration and washing, we find their virulence restored, so that the diminished virulence must be due to the specific action on the animal organism of a protective substance hidden in the serum. *Artificial immunity, therefore, depends neither on a "direct" germicidal nor on an attenuating power acquired by the serum and fluids of the protected animal.*

Although, while working in the laboratory with test-tubes and serum, we find that the protective serum itself is neither attenuating nor consistently bactericidal, nevertheless it is certain that the processes in the body are very different. There can be no doubt, in spite of Metschnikoff's objections, that when we inject cholera vibrios intra-peritoneally into a protected animal, crowds of them die in the peritoneal fluid without any direct interference on the part of the cells — without phagocytosis. Conversely if we administer the anti-diphtheritic serum to patients and examine their tonsillar or faucial membranes from day to day, we shall frequently find that legions of diphtheria bacilli die an extracellular death. Similarly after the pneumonic crisis, which marks the period of acquired immunity, the diplococci die in large numbers without direct conflict with the cells. Hence, though our test-tube observations may point the other way, we are forced to assume that during the process of recovery which ends in acquired immunity the body becomes so greatly altered that its tissues and fluids become not only antitoxic, but also germicidal. These are two distinct and specifically acquired properties which serve to protect the body when its immunity is threatened.

Hence the secret of an artificial specific immunity must be sought for in peculiar vital changes produced in the animal organisms by various processes, either actively or passively specific. An active immunity, as already explained, is produced by inoculation with living organisms and their products, the resistance being acquired after an active struggle against the causes of disease; a passive immunity is produced by the administration of the specific serum, the resistance being acquired, without an active struggle, by a peculiar modification brought about under the influence of certain specific substances. The chief difference between the unprotected and the actively protected animal is that the serum or tissue extracts of the latter possess a specifically immunising power. Since this change affects all tissues, it is evident that, as the animal passes from the susceptible to the immune state, we are dealing not merely with a modification of this or the other fluid or cell, but with a general reaction. Acquired immunity does not depend on resistance acquired by certain cells or elements alone; when once produced it finds expression in vital germicidal and antitoxic properties acquired by the tissues and their fluids. It is obvious that a struggle against pathogenetic bacteria can only end successfully if these are eventually destroyed, and their toxic products rendered harmless. The conception, therefore, of an acquired immunity depending on phagocytosis alone, is absurdly narrow and incomplete. The toxins being the most dangerous weapons of the bacteria, the antitoxic reaction of the tissues is no doubt the more important modification; but histological bacterioscopic and clinical investigations show clearly that with the appearance of immunity and recovery the micro-organisms also die. Their death is due (*a*) to action of the cells, or phagocytosis, but also (*b*) to extracellular destruction. Phagocytosis is therefore merely one factor of immunity, one, indeed, not invariably present, nor, when present, equally important in all cases.

It may be present although the animal die from the effect of intoxication. It is futile then, as we have seen, to enter at the present time into further discussion when the advances of our knowledge so clearly indicate the limitations of the phagocytic theory.

Artificial immunity, therefore, to state it once more, depends on processes which render the tissues capable of (*a*) destroying bacterial life, and (*b*) of rendering the products of bacterial activity inert; destruction of the bacteria themselves is not sufficient to save the animal, unless the toxins are also accounted for, or unless the bacteria are destroyed before they have time to form their toxins. It is conceivable that an animal may survive, if the poison alone be destroyed or rendered inert, but it is a matter of experimental as well as of clinical observation that antitoxic processes in the body are almost invariably accompanied by antimicrobic effects. A protected animal reacts to an infection with local inflammatory changes which soon pass off; the bacteria disappear without their products having had a fair chance of displaying their existence and activity. Inasmuch as phagocytosis is a common phenomenon in an inflammatory process, leading to resolution and repair, it will also show itself concurrently with immunity; but the essence or cause of immunity it cannot possibly be.

As yet we have no certain knowledge of these antimicrobic and antitoxic substances. It seems erroneous to assume that the germicidal serum or tissue extracts contain these matters in the form in which they subsequently appear in the animal body. It is more reasonable to assume that they are called into existence by the action of the serum, or of substances contained in the serum, on the tissues; this is certainly the case so far as the germicidal properties of the immunised tissues are concerned, for the protective serum in the test-tube but rarely possesses any such properties, while the animal body certainly does. Again, by means of chemical vaccination we render an animal refractory, so that its tissues are able, both by intracellular and extracellular action, to destroy the microbe, and yet this germicidal virtue is rarely transmitted to the serum. It has also been shown that after heating, which, as we know, removes all possible germicidal and antitoxic powers it may possess, the protective serum inoculated into an animal is still capable of conferring immunity to the tissues and their juices by virtue of which they are able to overcome a bacterial infection. With regard to the antitoxic effect it is still more difficult to come to a definite conclusion. At first sight we might ask why we should require a different explanation here? In almost all, if not in all cases, it takes a long course of inoculation with toxins to generate a weak antitoxic serum; but when the animal is once immune its total serum will give much more antitoxin than corresponds to the dose of poison against which it has been protected. Roux has further shown that the same quantity of toxin given in many small doses leads to a greater store of antitoxin in the tissues than when given in a single large dose. Lastly, we have the observations alluded to above, that a mixture of serum and toxin, apparently neutral for one group of animals, is still

toxic for more susceptible animals; or to put it otherwise, "clinically cure does not follow the introduction of the serum with the certainty and precision of a chemical reaction" (Welch). It is, therefore, in all probability incorrect to suppose that the protective serum has a "direct" antitoxic and germicidal action which it shares with the tissues; the changes, induced by the injected serum, which render the tissues and their fluids both antimicrobic and antitoxic, have a specifically vital character.

Buchner has made attempts to separate the antitoxic bodies from serum in a more definite form. All attempts to obtain them in a pure state have failed, and in the present state of physiological chemistry must fail. The serum may be dried *in vacuo* and still retain its remarkable properties; it may be precipitated by sodium-ammonium sulphate in the form of a highly antitoxic powder. Heat destroys the action of the antitoxins, but with some difficulty, they are resistant also to light and putrefaction, and in many respects they resemble the enzymes. Buchner's own view is that the antitoxins are substances directly derived from the bacterial plasma. There is, however, no definite evidence in favour of this assumption, and for the time being we must confess our ignorance of the nature of these protective and curative substances.

Whatever the nature of these so-called antitoxins of bacterial origin may be, their action is specific; that is, an anti-diphtheritic serum, from whatsoever animal obtained, will immunise against diphtheria alone. Most experiments, as I have said, tend to prove this point; and the recent attempt made, especially by the French school, to cast doubt on this proposition, does not as yet carry conviction. It is true that Calmette has shown not only that by gradually rendering animals proof against snake poison, their serum in this case likewise becomes protective and curative, but also that the serum of an animal inoculated against cobra venom will counteract the effects of the venom of other snakes; yet this exception is but apparent, as it appears from their physiological or pathological action that the snake venoms generally employed belong to one physiological group. Calmette, however, claims that anti-tetanic serum also works antagonistically to snake poison. But recent experiments show that this view of the absence of specificity rests on an insufficiently sound basis, and applies perhaps more to the antitoxins prepared for poisons of non-bacterial origin; so that the specificity of antitoxic serum, for infective lesions at least, cannot as yet be denied. The most important feature of the observations on snake poison is the fact, already demonstrated by Ehrlich, that what can be done against the bacterial toxins can also be effected against the chemically and physiologically allied animal or vegetable poisons. Attempts to obtain a protective serum against the vegetable alkaloids by means of gradually increasing inoculations have hitherto failed.

The view that the antitoxins are modified toxins or direct derivatives from the mycoproteins is disproved by Roux's experiments, who showed that a horse strongly protected against diphtheria toxin, if bled, gives a serum of certain value; if bled again a little time later, its serum will have the same value as that first removed, although no poison has been

administered in the meantime to raise the immunity. Hence, fresh antitoxin must have been produced without fresh inoculation with toxin. Antitoxin must, therefore, be a direct product of the cells by virtue of acquired secretory changes, and its action must also be directly cellular.

This sketchy and elementary survey of the subject of Acquired Immunity must suffice, since the whole subject is one which readily invites speculation which may hardly prove profitable, and would at any rate fall beyond the scope of a general article.

Natural Immunity. — While discussing predisposition we have frequently alluded to natural resistance and immunity, so that here a few brief remarks will suffice. Natural immunity, like predisposition, may be individual or personal, or may belong to all the members of a species or a race. Amongst animals, for instance, we find that Algerian sheep are resistant to anthrax, an infection very fatal to other sheep; and we have already commented upon the marked insusceptibility of negroes to yellow fever and ague, which amounts almost to immunity. Carnivora generally are distinguished by a marked degree of resistance to anthrax and septic infection, which is almost equivalent to exemption. Racial immunity to a great extent must have been acquired by natural selection and inheritance, as the more refractory members survive; and since the properties to which they owe their survival are of benefit to the species, we may assume that they are readily transmitted by heredity. The influence of bacterial diseases on the origin of species has not received as yet due attention, nor again this influence on the extermination of species. This is not the place to consider this question; but I may point out that there is sufficient historic evidence to suggest that continued exposure to an infection tends to establish a racial resistance, for we find that the commoner infective fevers when introduced amongst a population unacquainted with them, assume a most malignant and fatal form.

Natural immunity may be either absolute or relative according to its intensity. But few animals are absolutely immune, for in most cases it is possible to infect them, without otherwise interfering with them, by inoculating excessive quantities of bacteria into their tissues, or by introducing the germs in special regions of the body. An animal though able to resist large doses injected subcutaneously, may readily succumb to intra-peritoneal inoculations; while in other cases intra-peritoneal inoculations may be resisted when subcutaneous infection proves fatal. This opens up the broad question of local immunity, which at present is beyond the reach of an answer. A personal immunity may be merely temporary, and then it is often apparent rather than real. When we find, for instance, that during an epidemic a certain number of people remain intact, this exemption is not necessarily due to a natural insusceptibility, but in some cases may be explained by assuming (1) that there was no exposure to the contagion, or (2) that certain external conditions required for a successful infection were absent. An individual who has escaped during one epidemic may become infected subsequently; either because his immunity was only temporary, or because in the meantime he

has acquired the necessary disposition. We must draw a hard and fast line between temporary and relative immunity on the one hand, and loss of resistance on the other.

When an animal is naturally immune from a bacterial infection, it is also proof against intoxication, an important consideration, as we shall see hereafter, for no theory of immunity can be advanced unless it explains also this essential factor of natural resistance. The temporary or permanent immunity which some individuals enjoy may be due to the intolerance of poisons, especially when pathogenetic organisms find an abode in the body without producing an infection, as, for example, is the case with the pneumococcus, whose presence is borne with impunity by a large percentage of people. It is, however, also possible that such organisms while growing in the various secretions and excretions display but little or no virulence. Altogether we are on ground so very unsafe, and surrounded by so many fallacies, that it is wiser to attack the problem of natural immunity in its simplest form.

We find that some animals are refractory to certain bacterial infections, susceptible to others. How are we to explain this? Various views of the matter have been brought forward from time to time.

Theory of Natural Immunity. — (α) Metschnikoff preached phagocytosis, but we have already seen that in an exclusive form this theory is untenable, especially as in most bacterial infections we are dealing with the toxins as well as with the micro-organisms themselves. Again phagocytosis may be present to a marked degree, although the animal die (for example, diphtheritic infection in guinea-pigs). As in acquired so also in natural immunity phagocytosis is merely a phenomenon of natural resistance.

(β) It has been assumed, especially by Buchner and Hankin, that in the condition of natural immunity the blood, lymph, and tissue fluids are germicidal, and that this property is due to certain albuminous or albuminoid substances which may be separated in an impure form from the blood, spleen and other tissues of most animals. To these bodies Buchner gave the name of alexins. They are secreted by certain cells of the body, according to Hankin more especially by the leucocytes, and pass into solution. Certainly, as we have already seen, the serum of many animals has some germicidal properties, and from the spleen and lymphatic glands albuminous substances capable of destroying or impairing bacterial life can be removed. These so-called alexins differ from the antitoxins in these points: (i) they are very sensitive to light or heat; (ii) they have a distinct, though unequal, germicidal power, which (iii) varies both in intensity and effects with the species of the animal; in one species they are active against one microbe, in another species against another. There is in them no uniformity or common principle of action.

There are many weak points in such a doctrine, of which I may mention a few. Thus, the experimental evidence is unsatisfactory, since it rests mostly on test-tube reactions which often differ materially from those in the animal body. Frequently the serum shows slight antimicrobic

powers outside the animal body, while the living tissues exert no such power. Again, there is no complete correlation between natural immunity and this property of the serum, and without it the theory must fall to ground. Even in the most refractory animals the destructive power of the serum over the micro-organism is too slight to tempt us seriously to accept this theory. Thus, we find that frogs' serum in a test-tube will destroy but a very small percentage of the anthrax bacilli added to it, and that even this slight germicidal power is lost after a short time. There can be no doubt that the serum or plasma does contain such substances (or alexins, if we wish to use a mystic language); for the germicidal power, slight as it is, is readily destroyed by heat or cold. There are no doubt destructive substances in the blood of many animals, yet for the above reason it seems impossible thereby to explain natural immunity, especially since it has been found impossible hitherto to produce specific cures by means of repeated injections of such bodies. Again, the alexins have never been shown to have an antitoxic effect, and it is a matter beyond dispute that an immune animal is also toxin proof. But we must confess that the serum of certain refractory animals is antitoxic to snake poison; yet here again there is no constancy, since some venom-proof animals yield no antitoxic serum, while on the other hand some susceptible animals yield an antitoxic serum. Natural immunity, therefore, must depend on vital reactions which are called forth by the conflict between the tissues and the bacteria with their products, the final outcome being death of the micro-organisms and neutralisation of the toxins. The destruction of bacterial life is assisted by the innate germicidal and antitoxic power of the serum, plasma, or lymph found in many animals, and by the phagocytic properties of the wandering cells.

(γ) This reactionary vitality of the tissues and their cells may be increased in many ways. Thus, Wooldridge showed that the injection of thymus extract may protect rabbits against anthrax, and Kossel, Vaughan, and M'Clintock have rendered animals refractory to bacterial infections by the administration of nuclein and nucleinic acid. Since it requires in the case of susceptible animals a certain minimal number of micro-organisms to produce infection, it follows that every animal possesses the elements or the germs of immunity. These will destroy a certain number of bacteria, but if we pass beyond the limit, disease will occur. If now in one way or another we increase this innate resisting power by cell-stimuli, the animal will be able to resist a larger number; it will appear, that is, to be immune, or to have acquired an immunity. We may increase this innate resisting power in two directions: (*a*), specifically against a particular infection by administering repeated or increasing doses of the bacteria, their proteins, or their toxins; or (*b*), generally against all infections by giving such substances as nuclein, nucleo-albumins, nucleinic acid.

In either case we increase the reacting powers of the tissues; it appears, however, that only when we do so specifically we can obtain a protective serum. Thus, Hildebrandt has shown that by means of enzymes of various kinds we may alter animals to such an extent that they are

capable of resisting acute infections; yet if the serum of animals, which have been treated with ferments and enzymes, be injected into normal animals, it has no antidotal value. The enzyme injections, therefore, raise the natural resistance, but do not produce an immunity which can be transmitted from one individual to another by means of the serum.

We stand, therefore, before a question which we are quite unable to answer; namely, what is the difference between natural resistance and acquired specific immunity? The former is an innate property of the individual or species, one which cannot be transmitted, except by heredity, from parent to offspring; the latter is readily transferred from one individual to another by serum injections. Yet we find that by producing a specific transferable immunity the natural general resistance is frequently raised, for clinically it may be shown that recovery from an infective fever often renders the individual less susceptible to other infective fevers; occasionally, however, it may render the individual even more susceptible.

Hereditary Immunity. — An acquired specific immunity may also be transmitted from parent to offspring. Numerous experiments prove this, but the most important are those of Ehrlich, and of Tizzoni and his school. These observers worked especially with strong toxins, and while Ehrlich showed that immunity is exclusively transmitted through the maternal tissues, the Italians claim to have demonstrated that the transmission may also be through the spermatic fluid. Maternal transmission is hardly inheritance, since the fœtus is nourished by the blood and fluids of the mother; it is rather intra-uterine protection. Ehrlich has also shown that an immunity may be acquired through the milk of protected animals, so that sucklings may drink to their own protection at their mothers' breasts. Needless to say the action of the milk is specific. The importance of these observations, both as concerns the individual and society at large, will be readily seen. The results of Tizzoni and Cattani have not yet been confirmed, and on the other hand have been negatived by other observers, so that at present we may doubt the possibility of the germinal transmission. As in extra-uterine life immunity may be acquired through recovery from an infective process, so also the embryo or fœtus may gain protection after a successful struggle with a disease contracted *in utero*. In most cases, however, this protection is called into existence, or increased through the protective and curative substances developed in the mother. Amongst human beings an artificial specific immunity may be transmitted to the fœtus for small-pox and syphilis, which may be due either to a simple transmission of the maternal immunity, brought about through the protective circulation, or may be due to the fact that concurrently with the pregnant mother, the fœtus, sharing her blood, was impregnated with the antidotal substances introduced into or developed in the mother. The mechanism of immunity conferred by inheritance is as yet in obscurity.

Indeed the mechanism of immunity, whether acquired or natural, specific or general, is still hidden from us; and we cannot as yet lift the veil which is interposed between us and the facts. We cannot enter into all

the seductive hypotheses to which scientific enthusiasm gives expression: "from enthusiasm to imposture the path is perilous and slippery." We must therefore receive the discoveries of the day with the open and impartial mind of the historian, trusting that the future, perhaps the near future, will arrange them in their proper order and proportions, so that retrospectively we may learn their lesson. At present the thinker stands bewildered before the problem of immunity; and when two recent writers (Freund and Grosz) assert that a close relation appears to exist between the process of coagulation and serum immunisation, we may remember that we are equally ignorant of the inner working of either process. It is because of these limitations of our understanding that I have passed over numberless observations, such as local immunity, or the production of immunity by bacteria or chemical substances not specifically related to the disease in question. Yet the recent past has revealed so many marvellous facts unto us that we may confidently look to the future for more light.

Serum Therapeutics

If any arguments be needed to justify those high aims of the pathologist or bacteriologist which are attained through the sacrifice of animal life in carefully devised experiments, we may point with pride to the number of lives saved by means of the treatment with curative serum; this treatment, great even in its present success, and based on sound experience and observation, invites us to expect more success in the future than the past has already given us. The principles of the new therapeutic method have been fully discussed in the previous pages. It is founded on the generally established fact that susceptible animals, adequately protected so as to reach the highest possible degree of immunity from infections with pathogenetic bacteria or from intoxications with their chemical products, are capable of supplying a serum which, injected into other susceptible animals, will protect them also against like infections or intoxications; and, even when injected after the earlier symptoms of the infection or intoxication have appeared, may determine the cure of the diseased animals. Obviously it requires larger doses to remove a lesion than to prevent an infection or intoxication. Experimental work has further shown that the serum of one animal will display this specific activity in animals belonging to widely different species. The practical and clinical application of these laboratory observations has opened up a new method of treating bacterial and toxic lesions, which consists in the injection of curative substances obtained from the blood of highly protected animals into the diseased individuals; and since these substances are contained in the serum, this therapeutic method is called the "serum treatment." These specific substances may be kept in a stable and durable form, either in the form of liquid serum, or in the dried state after desiccating the serum *in vacuo;* so that they may be used as quantities measurable by weight or volume and constant in potency.

Behring had first shown that, as far as animals are concerned, this method is followed by successful results in tetanus, diphtheria, and the various streptococcus infections. Now these lesions differ greatly in principle: tetanus is an acute intoxicative process of the most rapid development; diphtheria resembles it, but is less rapid; the streptococcus infections are less intoxicative, and in their severity depend chiefly on the distribution and growth of the micro-organisms themselves: these also have a marked tendency to infect the blood and the tissues generally, while the tetanus bacilli always, and diphtheria bacilli generally remain at the seat of inoculation, multiplying to a limited extent and manufacturing their more active poisons. Thus we have learned that a curative serum may be prepared for intoxicative as well as for infective lesions of bacterial origin.

The next step was Ehrlich's discovery that Behring's principle may be employed also in the treatment and protection of animals against poisoning with vegetable toxalbumins, such as abrin and ricin. The field and scope of the serum treatment thus at once became, fundamentally at least, much wider and more promising. How far-reaching are these earlier observations we have now realised on Calmette's demonstration that it is possible to render animals proof against snake venoms, and to obtain from these animals a serum, capable of protecting other, even highly susceptible animals, against the poison; and powerful enough to save them even when the first symptoms have already appeared. These toxic bodies are not of bacterial origin, but they bear close resemblance to the mycotic poisons. Attempts to prepare a serum antagonistic to the recognised chemical poisons, inorganic, organic, or alkaloidal in nature, have utterly failed, so that there is a near limit to the scope of the serum treatment, even in the laboratory; it seems that only certain substances of distinctive chemico-physiological action are capable of producing the kind of reaction in the animal body which results in the formation of antitoxic substances. We have some grounds for suspecting a correlation between chemical constitution and physiological action in other branches of therapeutics and pharmacology; and some such principle, at present obscure, may underlie both the changes produced in the animal organism when protected against so-called toxalbumins and enzymes, and those which happen in the case of the alkaloids which are bodies of entirely different chemical structure.

The curative value of a serum varies directly as its protective power, so that to obtain an active serum the animal must be endowed with the highest possible degree of immunity. Since in every animal, according to its size and susceptibility, there is a limit beyond which its immunity cannot be pushed, the larger animals, such as horses, must be used for the purpose of obtaining a curative serum. These must be treated by methods which will result in the shortest possible time in the strongest resistance obtainable without damage to their tissues.

Broadly speaking, there are two methods by which the animals may be prepared. Firstly, they may be inoculated with gradually increasing doses of the toxins; secondly, they may be treated with the living or dead bodies of the bacteria, also injected in gradually increasing quantities.

The increase must be gradual, because the animal acquires resistance gradually, and our aim must be to get as near as possible to the maximum immunity, and then to keep it at this level. If from time to time we remove blood from the animal under preparation, we shall find its serum gradually increasing in protective power. Behring and Ehrlich have suggested the following as a standard of value. In the case of anti-diphtheritic serum, a serum 0·1 c.c. of which when mixed in a test-tube with ten times the fatal dose of diphtheria toxin is capable of rendering the latter harmless to a guinea-pig weighing about 300 grammes, is taken as the standard, and is called "normal serum." 1 c.c. of such serum is the protective unit, so that, for instance, a serum of which 0·01 c.c. suffices for complete protection possesses ten units. Roux's standard differs from that of the Germans. His constant is a toxin solution of which 0·1 c.c. kills a guinea-pig weighing 500 grammes in 48 hours. If 1 c.c. of this toxic solution be rendered harmless by 0·05 c.c. of serum, then evidently 1 c.c. of serum is capable of protecting 100,000 grammes of guinea-pig against 0·1 c.c. of toxin; hence the protective value of such serum is 100,000. By his method of protection, which consists essentially in injecting toxins, Behring has succeeded in obtaining an anti-diphtheritic serum of 600–1500 units. During the artificial protection of animals it is regularly found that each injection is followed by a marked reaction, during which the temperature rises, the weight falls, and the animal is ill. During this period of reaction the immunity, and therefore also the protective value of the serum, is considerably lowered; but when the animal has recovered both are considerably raised. Hence the protective inoculations should not be made during these periods of reaction, nor should the blood of the animal be taken for therapeutic purposes until it is well and sound again. While administering diphtheria toxins to horses it has frequently been found that at first the antitoxic value steadily ascends, but that when large doses of toxins have been reached this value decreases. This would seem to show that in the eagerness of obtaining a potent serum the protective substances stored up in the animal organism have been overtaxed; or, to express it in other words, the animal having been brought to the limit of its immunity, inordinate demands have been made on its own antitoxic substances by injecting enormous doses of fresh toxin, in the hope of raising its immunity indefinitely. There is, however, a point beyond which we cannot go.

Dr. Klein established an important fact when he showed that an anti-diphtheritic serum, obtained after toxin injections, attains to a high degree of antitoxic potency, but to a lower degree of protective potency than a serum obtained after injections of living cultures. Further, he showed that by administration of living cultures the same degree of protective power is acquired by horse's serum in a considerably shorter space of time than after repeated toxin inoculations. It follows that for the preparation of the most useful serum the injection of toxin in increasing doses should be combined with inoculations of living bacteria; for in this way a serum possessed both of highly antitoxic and preventive

virtues might be obtained. In disease as it appears in man, we have to deal both with the poison already produced and with the bacteria capable of producing more; it must be our aim, therefore, to attack the sources of disease on all sides, at any rate in such lesions as diphtheria where the bacilli, although they are generally localised in the membranes, are nevertheless extremely numerous; in the case of tetanus and *à fortiori* in snake poisoning we require merely a highly antitoxic value.

If now we shortly review the scope of the serum treatment, we find (1) that every infection requires for its prevention and cure a specially and apparently a specifically prepared serum. We have already referred to the attempt made by Calmette to shake this law, perhaps too exclusively conceived by Behring, and we have seen that, so far as bacterial diseases are concerned, the law still holds good. In fact, from a practical point of view, this very specificity of the curative serum must limit its application. Thus Pfeiffer has shown that although the various vibrios obtained from choleraic dejecta are closely allied, and morphologically and biologically frequently inseparable, yet each special form of vibrio has its own anti-choleraic serum; a protective serum prepared against one variety is not necessarily antidotal to another. In cholera the clinical lesions are uniform and characteristic, but they may be caused by several closely allied forms of vibrio. Accordingly, we find that it is not possible, in the laboratory at any rate, to obtain a universal anti-choleraic serum. Again, both staphylococci and streptococci produce suppuration, septicæmia, erysipelas and pyæmia; and although with our clinical imperfections we are unable to detect essential differences, or any at all, between processes associated with one or other group of cocci, yet a serum antagonistic to an infection by one is useless against infections by the others. It seems, then, that in the treatment of infective diseases by this new method conditions seem most favourable in those specific cases — such as tetanus, diphtheria, enteric fever — which, in their uncomplicated form, are due to a single organism. In other cases, such as cholera, suppuration, and septicæmic lesions, obvious difficulties must arise in the uncertainty and diversity of the bacteria flora.

(2) Specific curative effects cannot be attained by means of blood of refractory animals in their normal state, that is, not specifically protected. In this direction laboratory experiments have invariably led to failure. Richet and Héricourt, and others, claimed to have discovered powers curative of tuberculosis in the serum of goats, sheep, and dogs, animals almost absolutely refractory to this microbe. Experimentally, however, the blood of these animals has been shown by Bouchard and others to be devoid of protective power, and it follows therefrom that it is devoid of curative power.

(3) Since the action of the curative serum is specific, we cannot expect it also to counteract any secondary infections by other organisms. Thus, in diphtheria, complications due to the interference of pyogenetic cocci, especially streptococci, are not infrequent; against these the anti-diphtheritic serum is powerless; it can counteract the effects

of diphtheria bacilli and their toxins, but of these only. The secondary infections must be dealt with by other means, it may be by injections of serums specially prepared for these cocci, it may be by vigorous means of general disinfection.

(4) In all cases an adequate dose of antitoxin serum is to be administered. Now, as the dose of toxin present in a patient, and the number of bacteria settled in his tissues cannot be estimated, it is of importance not to use too little of the antidote, and rather to force the treatment than to remain more or less expectant. Both in the case of tetanus and diphtheria copious dosage at frequent intervals has led to the best results. Of course in cases of slight severity less serum and a less energetic treatment is required than in graver cases. Many failures in the treatment of diphtheria have undoubtedly been due to inadequate dosage.

(5) By the researches of Calmette, mentioned above, the scope of the serum treatment has been considerably enlarged. Having succeeded in rendering animals so firmly resistant against snake poison as to obtain a highly antitoxic serum from them, he further showed that the serum active against the venom of one serpent is also potent against that of another. Herein he has been confirmed by Professor Fraser of Edinburgh and others. The future must show how far these observations are applicable outside the precincts of the laboratory.

(6) The antitoxic treatment has hitherto been tried in man in several diseases, and a short summary of results may be acceptable at this point. Its success is so undoubted in diphtheria as to silence all opposition, and to lead us to hope for better and better results. It is a specific remedy, and it surpasses any other which has ever been employed for the treatment of this disease.

The anti-tetanic serum has, unfortunately, been less successful; chiefly because of the extraordinary severity of the disease against which it is employed. In acute cases with a short incubation period and a rapid onset of spasms it has so far been useless; but chronic cases with a long incubation period and a slow onset of spasms seem to be benefited [*vide* art. "Tetanus"]. These latter cases, however, frequently do well under other methods of treatment. Again, under ordinary circumstances treatment is begun too late, and the prospect of success is therefore not very hopeful in any really serious case.

Attempts have been made to cure pneumonia, erysipelas, puerperal fever, pneumococcus meningitis, typhoid fever, and also cholera in the human subject by means of injections of a specific serum. The facts which we possess as yet are too meagre for discussion; yet so much has already been achieved by careful observation in the laboratory that further triumphs may be confidently anticipated. Success, however, cannot be forced: one serum after another has been vaunted as a curative agent in tuberculosis; the dog, the goat, and the ass have had false pretensions thrust upon them; and recently Maragliano has come forward with an anti-tuberculous serum, which, however, is evidently not a true antitoxic or immunity-conferring serum: it seems rather to act as a

modified tuberculin, raising the temperature considerably on injection, and producing other physiological changes as a rule not observed with protective serums. Moreover, Maragliano's observations are not based on sound experiments; he fails, at any rate, to record any successful preventive inoculation of susceptible animals. Our great difficulties in tuberculosis are the protection of the individual from secondary infections, and the removal of the latter when they have once made their appearance.

In conclusion a few words must be said on the dosage and administration of curative serum. Carefully prepared and preserved it is harmless; and local inflammation or suppuration, if they appear, are generally due to a contamination of the serum during its use, or to want of asepsis in the injection of it into the tissues. Cleanliness is an imperative necessity, although local infections are excessively rare. The serum may be obtained either in a liquid or dried state; in the latter case a certain weight of it must be carefully suspended and ground up in sterile water, or saline solution, or sterile camphor, or thymol water. The dried serum will dissolve only in part: after shaking it vigorously it is allowed to stand, in order to allow the insoluble matter to fall down. The water extracts the active principles and holds them in solution. The skin at the seat of injection must be carefully washed and cleansed with antiseptic lotion, and the syringe boiled before use; a proper instrument which can be readily sterilised must be chosen.

The injections should be made into the subcutaneous tissues of the flanks or buttocks, and *as soon as possible;* a day's, nay a few hours' delay may mean the patient's death: the prompter the treatment the greater the chances of success. The quantity of serum to be used, as already explained, varies with each case, with the strength of the serum and the age and weight of the patient; but as a rule in a severe case it is advisable to administer the antitoxin boldly. If, as in the case of tetanus, large doses (up to 100 c.c.) have to be injected, the quantity must, of course, be distributed over different places; more than 25 c.c. should never be injected at any one spot. After use the syringe and needle must again be thoroughly cleaned, first with sterile water, then with alcohol, and lastly with ether.

Although we possess in the antitoxin a remarkable therapeutic agent, we must not in our enthusiasm forget older established methods. Thus in the case of diphtheria local antiseptics and tonics should be employed as far as possible; in the case of tetanus physostigmin and other drugs, and operative treatment must not be neglected. There is no reason why we should disregard measures of a useful kind which may hasten recovery by removing the source of infection.

Rashes occasionally occur after the administration of serum, generally of erythematous or urticarial character; they appear either around the seat of injection, or they may affect the whole body, or certain areas of it, especially the extensor surfaces of the limbs. These eruptions are produced by substances in the serum other than the specific antitoxic substances, since they may occur on injecting normal horse's serum;

undoubtedly in time they may be eliminated, indeed it appears that on using dried serum they are less frequent.

Joint-pains are also said to occur occasionally; there may be redness around the articulation, and even effusion into the synovial cavity, the hips, ankles, and wrists being most frequently affected. No ill result of these complications has ever been recorded, but they retard recovery; it must be our aim, therefore, to obtain a serum free from such contamination. Serious harm, such as nephritis or suppression of the urine, never results, — although statements have been made to the contrary. Dr. Caiger speaks emphatically on this point, and we may take it for granted that, given a pure serum-supply, care in administration, and responsible circumspection, all serious complications can be avoided.

It has already been mentioned that the protective value of curative serum, at least so far as our laboratory animals are concerned, is very high, even although the immunity produced is only temporary. Frequent proposals have been made by Behring, Roux, Vaillard, and others, to use the antitoxin for purposes of prevention in the case of diphtheria and tetanus; so far, however, this suggestion has not had the recognition it undoubtedly deserves. Behring, in fact, expects that "by the combination of prophylactic and actual treatment with antitoxic serum, we must eventually succeed in abolishing diphtheria and in confining it to the pages of history." In local epidemics of diphtheria serum protection might be practised; and, although tetanus is a rare disease, protective injections are also advisable in cases of wounds contaminated with sand, earth, or dust: prevention is frequently easy; cure may be impossible. It is fair to add, however, that the protective value of the antidiphtheritic serum, in man at any rate, does not seem to be considerable.

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SEPTICÆMIA AND PYÆMIA

Introduction. — Under this general heading are usually included three constitutional affections which, both pathologically and etiologically, are quite distinct. Speaking broadly, it may be said that they are due to the entrance into the general system either of micro-organisms or of their products; and as a rule they are met with in connection with some wound or breach of surface, the discharges from which have become contaminated with bacteria. Three different results may follow the entrance of bacteria into a wound, and it is not uncommon to find two or more of

them in combination; indeed, in the great majority of cases the condition of sapræmia accompanies that of septicæmia or pyæmia.

The first of these affections is *sapræmia*, which is also spoken of as septic or putrid poisoning or intoxication. Sapræmia is a general constitutional disorder exclusively due to chemical poisoning by the products of bacteria, and not to the entrance of the bacteria themselves into the blood. The poison so introduced cannot increase in the system except by the absorption of fresh doses; and the blood of an animal that has died of the disease only contains a diluted solution of the amount of poison it had received, so that small quantities of this blood, when injected into another animal equally susceptible, will not set up symptoms of poisoning. Hence the disease is in no sense an infective one; moreover the poison absorbed is being so constantly and rapidly eliminated from the system that, provided the dose already taken up be not a fatal one and that all further supplies are stopped, the disease will of itself come to a spontaneous and favourable termination.

The second form of septic disease, *septicæmia*, or septic infection, is a disorder caused not only by the absorption of poisons from a wound, but also by the entrance of living micro-organisms into the body and their growth and multiplication therein. Although in this case, as in sapræmia, it is probable that the constitutional effects are due solely to the chemical poisons produced by the organisms, and not to the presence of the organisms themselves in the blood stream, yet there is this cardinal difference, that in septicæmia the poison is being continually produced inside the body; whereas in sapræmia the poison is produced in the wound — that is to say, outside the body — and is absorbed from that part. Hence it generally happens in the case of septicæmia — in contra-distinction to sapræmia — that, if the disease be firmly established, it cannot be moderated by the removal of the original source of infection.

Thirdly, we have to consider *pyæmia*, an acute, general, infective disease, due to the entrance of living pyogenetic micro-organisms into the blood, and especially characterised by the formation of abscesses in various organs and parts of the body. Here we have not only poisoning of the body with the products of micro-organisms which have already established themselves in the living body, but we have in addition the occurrence of septic emboli, either the result of suppurative phlebitis or thrombosis, or formed in other ways which will be afterwards discussed; these give rise to the abscesses characteristic of the disease.

By some authors a second form of pyæmia is spoken of under the term *Chronic Pyæmia*. This is a disease which arises also in connection with wounds, which is caused by pyogenetic organisms, and, like pyæmia proper, is characterised by the formation of local abscesses in various parts of the body. These abscesses, however, are fewer in number than in true pyæmia; they chiefly occur in subcutaneous tissues or joints, and apparently they are not due to embolism. For my own part, I prefer to designate this disease by the name "Multiple Abscesses;" for, except that it is due to pyogenetic organisms, it differs widely from pyæmia in its pathology, and should not, in my opinion, be described as a variety of this disease.

So much for definition; but, while for this purpose they are described as quite distinct from each other, it must be confessed that in practice it is not always easy—even at the post-mortem table—to assign definitely its exact part to each of the three forms in the production of symptoms; for, as I have said, two or more of them very often concur. The sharp separation between the three forms depends more on the results of the experiments on animals than on clinical observation; it may be interesting, therefore, to refer shortly to the experiments which have established the pathology of these affections.

Sapræmia.—At the beginning of this century Albert von Haller, Gaspard and many others, injected infusions of putrefying meat and other putrid animal fluids into animals, and observed the poisonous effects. They did not, however, attempt to determine the particular constituents on which these effects depended, and Panum was really the first who thoroughly studied this side of the subject. He showed that the poisonous properties of putrid solutions were unaltered by boiling, which would of course destroy all living elements; further, he found that the poison was in solution in the material, and he was able to separate substances in the form of a powder from putrefying materials which produced all the symptoms that occurred when the raw material was employed. This was done in the first place by filtering the fluid, and then adding absolute alcohol until a precipitate was obtained. This precipitate was collected and further purified by repeatedly dissolving it in distilled water and reprecipitating it. Finally it was dried at a temperature of 100° Centigrade. Even this treatment by alcohol, heat and drying did not destroy the poisonous products, 0·012 grammes of the powder so prepared being sufficient to kill a large dog.

Selmi attempted to carry the investigation further in order to determine the nature of the substances present in this powder; and he described a number of different substances, or more probably groups of substances, which he had isolated from putrefying animal tissues. To these substances, some of which were harmless and some intensely poisonous, he gave the name of animal alkaloids or ptomaines, these substances being transition products formed by the breaking up of the highly complex organic molecule on its way to form simple inorganic substances. Brieger has also thoroughly investigated this subject, and has isolated and named a number of these ptomaines, such as putrescine, cadaverine, neurine, etc. The organisms which produce these substances are not as a rule pathogenetic, that is to say, they are not as a rule able to live in the animal body. In cases in the lower animals (and also in man) where this intense poisoning has resulted, the organisms are not necessarily present in the blood during life, unless, indeed, the condition of sapræmia be complicated with some infective condition such as septicæmia.

When a quantity of putrefying material is injected into an animal—say a dog—in sufficient quantities to kill the animal, the most prominent symptoms are fever, vomiting, and diarrhœa: great restlessness and muscular twitchings may occur at first, but are soon followed

by loss of muscular power; the diarrhœa becomes profuse, serous, and frequently blood-stained, and is accompanied by much pain and tenesmus; the temperature falls, and usually becomes subnormal; the respiratory movements become very feeble; the pupils are dilated; there is marked cyanosis, and death ensues, apparently from cardiac failure. A fatal result usually takes place within twenty-four hours, depending directly on the dose injected and on the size and susceptibility of the animal. Koch describes the symptoms in mice as follows: — "The animal becomes restless, running about constantly, but showing great weakness and uncertainty in all its movements. It refuses food, respiration becomes irregular and slow, and death takes place in four to eight hours." When a smaller dose is employed the effects are similar but less severe, and the animal after a few hours rapidly recovers.

On post-mortem examination in these fatal cases we find no very prominent characteristics. Rigor mortis is transient and slightly marked; decomposition sets in early; there is no inflammation of the tissues in the neighbourhood of the site of injection. The chief changes occur in the blood, which is dark in colour, coagulates slightly and very imperfectly, and stains the lining wall of the veins and endocardium. Occasionally serous effusions are met with in some of the serous cavities, and these are also blood stained. Small, dark extravasations of blood are also commonly seen beneath the skin and serous membranes, and occasionally elsewhere throughout the body; the spleen is greatly swollen, often pulpy and dark, from engorgement with blood; there may be signs of severe gastro-enteritis with intense inflammation of the mucous membrane of the stomach and intestines, and with partial or almost complete desquamation of the epithelial lining (Burdon-Sanderson). Microscopical examination of the blood shows that the red corpuscles tend to form clumps instead of the usual rouleaux; it is found also that the staining of the vessel walls depends partly, at least, on the fact that many of the red corpuscles are disintegrated, and their liberated hæmoglobin is contained in solution in the blood plasma.

Septicœmia. — Koch, in confirmation of Panum's experiments, found that if a considerable quantity of putrefying blood were injected into animals, poisoning of the animals advancing to a fatal result was brought about; the blood of the animals so killed did not contain any bacteria, and was not capable of transmitting the disease. He further found that the rapidity and severity of the result were proportionate to the amount of putrid material injected; but when small quantities (one or two minims) of putrid blood were injected into mice, although no immediate symptoms were produced, yet in about one-third of the cases evidence of disease appeared within twenty-four hours, and if so a fatal result usually ensued. The same events also took place where much smaller doses were employed, but in this case the proportion of animals affected was still less.

The symptoms so set up were as follows: — After about twenty-four hours greatly increased conjunctival secretion came on which appeared to

glaze the eye, and ultimately glued the lids together; the animal soon ceased to eat, appeared overcome with lassitude, and moved but little; soon it sat still with its back bent and its legs drawn up; the respiratory movements were slow and feeble; the weakness increased, and death slowly ensued in forty to sixty hours. On post-mortem examination there was slight œdema at the site of the injection; the spleen was considerably enlarged, but no other marked changes were found except in the blood. Under a high power of the microscope numerous extremely minute bacilli were found in the blood, some free, others filling up the white corpuscles. The minutest quantity of this blood inoculated into a healthy mouse led to the disease, which was therefore a true infective one. Koch was subsequently able to cultivate these organisms, and the disease resulted from the inoculation of the cultivated organisms in the same way as from the inoculation of the blood.

Since this time a number of organisms have been found which produce similar symptoms in various classes of the lower animals; thus, in the case of rabbits, at least three different kinds of organisms set up these symptoms. This disease in the lower animals is spoken of as septicæmia, and is looked upon as the counterpart of septicæmia in man; but, in human septicæmia, as will be presently pointed out, organisms cannot be demonstrated in the blood in numbers at all comparable to those in the lower animals, or indeed in sufficient numbers to account for the disease, supposing it to be a simple blood infection.

Pyæmia. — In the course of Koch's researches on mice and rabbits he came across an organism which produced the condition comparable in these animals to pyæmia in man; and he found that this condition was due to the development of micrococci in the blood. It differed from human pyæmia in not being associated with thrombosis and embolism of portions of the thrombus, but that similar plugs were formed in the vessels in another way, which is also of interest in connection with human pyæmia wherein it is possible that something similar may take place. He found that this organism grew in the blood, and formed colonies in which masses of red blood corpuscles became incorporated; in this way emboli were formed which stuck in the smaller vessels. Another way in which a similar result was produced was that the organisms seemed to attach themselves to the endothelial cells, and, growing there, ultimately filled up the lumen of the blood-vessel and formed a plug. It is possible that a similar thing may occur in man, more especially in connection with the streptococcus pyogenes. Numerous experiments have also been made to determine the part which embolism plays in the production of pyæmia, but I may leave the reference to these until we come to speak of the pathology of pyæmia in man.

The clinical characters of these diseases as met with in practice must next be briefly described.

They may occur in connection with surgical operations, injuries, or diseases. Pure acute sapræmia, as above defined, is rarely found in surgical practice, and can only occur in the cases of large wounds or

cavities, such as the peritoneum, which are imperfectly drained; but it probably is not uncommonly seen in a milder form, and plays a part in the traumatic fever which so usually accompanies a septic wound. Hectic fever may be either a chronic sapræmia or a chronic septicæmia; that is to say, it is a state in which small doses of septic poison are constantly being absorbed either from the wound or from the tissues in which the organisms are situated. Septicæmia may result from wounds of any size, even from mere scratches if they happen to be infected with the necessary virus of sufficient virulence. Pyæmia may also result from wounds of any kind, or from surgical diseases associated with suppuration. Usually thrombosis occurs in the veins leading from the affected part, and the emboli resulting from the breaking down of the thrombus lodge in the first capillaries at which they arrive; consequently in most cases, where the systemic veins are affected, the lungs are the chief, or, it may be, the only part attacked. Pyæmia following acute osteo-myelitis is of the same type and due to the same causes; and although commonly described as a distinct variety of the disease it presents no special characteristics. The same may be said of the rarer cases occurring in connection with cellulitis, local abscesses, etc.

Puerperal fever, again, can no longer be considered as a separate disease. The uterus after parturition or abortion presents a large raw surface exactly comparable to that of a recent wound; and any of the forms of septic disease, or any admixture of them, may arise as the result of the retention of decomposing materials in its cavity, or of infection of the discharges. It may, however, be here noted that in these cases there is a special liability to the retention of a large mass of putrefying material in contact with a large absorbing surface, so that pure sapræmia is more often found in this than under any other conditions [*vide* art. on "Puerperal Septic Disease"].

Ulcerative, infective, or malignant endocarditis may occur in the course of an ordinary pyæmia, or may appear to be the starting-point of the disorder. In either case the pathological picture is peculiar, in that the primary affection occurs, in the great majority of cases, on the left side of the heart; thus the emboli given off from it lodge in the systemic arteries or capillaries, and lead to a true arterial pyæmia (Wilks). Beyond this, and the fact that the emboli are usually in great abundance, and that the lungs are not affected in the first instance, this disease does not differ from ordinary pyæmia [*vide* art. "Infective Endocarditis"].

Suppurative Pyle-phlebitis is a true pyæmia, where the original site of infection is situated somewhere in the area drained by the portal system of veins. It is then in the radicles of these veins that thrombosis occurs; and the resulting emboli will lodge, in the first instance, in the portal veins or capillaries of the liver. It may, in short, be accurately described as portal pyæmia. A rare form of this disease is occasionally seen in the newly born, and is sometimes described as umbilical pyæmia. It results from suppurative phlebitis of the unobliterated umbilical vein.

Idiopathic or spontaneous pyæmia and septicæmia are names applied

to those cases which present the ordinary clinical features and post-mortem appearances of this disease, but in which the source of the infection cannot be discovered. These cases will be further discussed later, but it may be here remarked that most of the published cases seem to be examples of multiple abscesses rather than of true pyæmia.

Infective myositis, an exceedingly rare disease characterised by multiple abscesses in the muscles throughout the body, has also been classed under pyæmia, but its pathology has not as yet been properly worked out.

A. Sapræmia

Etiology in Man. — The following conditions may be taken as necessary factors in the production of this disease in man: (1) There must be a large mass of dead material, whether injured tissues, blood-clot or discharge, which is undergoing putrefactive changes; (2) This putrefying material must be in contact with a large, rapidly absorbing surface such as would be furnished by a fresh wound, a serous surface, and the like; (3) Tension in the wound. keeping the discharges under pressure, and mechanically aiding their absorption.

It may also be accepted that the poisons will produce greater effects, or, conversely, that a smaller dose will be required, in persons who are debilitated, who are at either extreme of life, or in whom the excretory functions, which play so important a part in the elimination of the poison, are in any way impaired.

These demands will be satisfied by such conditions as the following: After parturition or abortion, portions of placenta, membranes, or blood-clot, if retained in the uterus, are very apt to become infected with putrefactive organisms and to undergo rapid decomposition. The interior of the uterus furnishes a large, raw, rapidly absorbing surface, so that a large dose of the poison must be absorbed. In many cases, also, the patient may be suffering from a certain amount of physical exhaustion or mental distress which renders her more susceptible to the poisonous influence [*vide* art. on "Puerperal Septic Disease"]. In surgical practice it may be met with after severe injuries, when a large, deep wound contains gangrenous tissue, blood, or discharges undergoing decomposition; also after operations when large cavities are left, as after the removal of large tumours, or the serous cavities of the pleura, peritoneum or large joints are laid open, and a quantity of decomposing material is pent up in an ill-drained cavity. Again, if a large chronic abscess—such as a psoas abscess—be imperfectly opened and drained, and putrefactive bacteria gain access to it, sapræmia may occur; and when in these instances it does occur, the symptoms set in very shortly after the injury — within a few hours.

It has long been known to surgeons, and especially urged by Sir Joseph Lister, that absorption does not take place, or at any rate but imperfectly, after a wound becomes completely covered with healthy granulation tissue; hence it is that the traumatic fever, the result of

septic absorption, comes to an end about the fourth or fifth day. It may be said here that cases of sapræmia at all comparable to those artificially produced on animals, or to those occurring in obstetric practice, are rare in surgical practice. In a special report on the subject of septic diseases to the Pathological Society of London 156 clinical records are published, and in 28 of these there were no metastatic abscesses. Of these 28 only two are considered cases of sapræmia, and even these are not beyond suspicion; it may fairly be urged, however, that these statistics do not give a complete view of the facts, for in a large proportion (24 out of the 26 remaining) septic poisoning, which could not be excluded, probably played some part in the production of the symptoms and fatal result; and, secondly, the statistics deal only with fatal cases, and this disease, as is well known, is overcome by proper treatment in a large proportion of cases.

But while acute and pure cases of sapræmia are rare, mild cases are commonly seen; it probably plays a great part in the so-called traumatic fever, that is, in fever occurring on the second or third day after injuries or operations, where sepsis has been allowed to take place in a wound. These mild cases are important from another point of view; the poisons irritate and set up an unhealthy state of the wound, and from their debilitating action on the patient they so lower the resisting powers of his tissues as to make him far more susceptible to the graver forms of septic infection.

Sapræmia, again, is not uncommon in operations on the peritoneum; and there can be no doubt that a good many of the cases of death from exhaustion, and of those cases where there has been fever but no peritonitis, are really cases of sapræmia due to the introduction of non-pathogenetic saprophytic organisms into the peritoneal cavity. Further, the poison being a chemical one, it may readily be absorbed from the alimentary canal; and it may be remarked that some of the symptoms following strangulation of the gut or intestinal obstruction, usually ascribed to collapse or recurrent shock, are in all probability due to absorption of poisons generated in the intestinal tract above the obstruction.

Symptoms. — The symptoms begin suddenly, and usually appear within twenty-four hours of the time that the discharges from the wound were noticed to be putrid. The temperature rises abruptly to 103°, 104°, or sometimes even higher, being accompanied, but by no means invariably, by a rigor. This initial rigor may be very severe, lasting half an hour or more, and usually is not repeated; in exceptional cases, however, repeated rigors may occur. At the same time the skin becomes hot, dry and flushed, the patient complains of intense headache, the tongue becomes coated with white fur, and there is intense thirst. Anorexia is complete; vomiting is common, and may be severe even from the commencement. Other common febrile symptoms also appear: the pulse is rapid and full; the respirations are hurried; the urine is scanty, high-coloured, and deposits urates on cooling. Locally a sufficient cause for the above symptoms is usually obvious. The wound may show

signs of inflammatory disturbance, or even appear gangrenous; and in all cases there is a considerable amount of very foul smelling discharge.

If the case be a severe one, and treatment not immediately adopted, signs of severe prostration rapidly supervene. There is delirium, especially at night, at first noisy but soon assuming the low muttering type, and becoming almost constant. There is excessive muscular weakness as evidenced by tremors. The tongue is now dry, brown and very tremulous; the mouth and lips are covered with sordes. Diarrhœa may come on, and motions and urine be passed unconsciously. The skin may be slightly jaundiced and petechiæ may appear. The temperature may fall, even to subnormal; coma comes on and gradually deepens into death. Death usually occurs about the second or third day of the disease; but in other cases may be postponed for as long as a week, the patient passing into a typical "typhoid state," and dying of exhaustion.

In less severe cases, those most commonly seen in surgical practice, the symptoms are similar but less marked. Usually improvement follows at once when the wound is freely opened, the putrid material removed, and free drainage established; but all fever may not cease until granulation is complete, and has formed an efficient barrier against further absorption. Even in the most severe cases recovery rapidly follows removal of the cause.

A brief abstract of a case quoted by Dr. Matthews Duncan may be given here, as it serves well to illustrate some of the more marked features of this disease. It is in every respect a pattern case, and indicates the happy result that may be anticipated if treatment be properly carried out.

"A young woman after a natural labour gave birth to her second child. For the first week slight bleeding took place, and on the seventh day the discharges were noticed to be putrid. The following day, the eighth, rigors occurred, and these were repeated daily until the eleventh day after delivery. The patient was then noticed to be very pale, frequently sick, and there was profuse diarrhœa. The uterus was tender, the breath sweet, respirations 44, pulse 146, temperature 104·2° F. The lochia were copious and stinking. She had been delirious all the previous night. Chloroform was administered, and large pieces of decomposing placenta removed from the uterus, which was thoroughly irrigated. The next day the patient had slept well without delirium, pulse 100, respirations 36, and the highest temperature 101·4°. Recovery henceforth was uninterrupted." Dr. Duncan remarks, "In twenty-four hours the whole aspect of the case changed from despair to hopefulness. The woman was at the point of death, it was apparently not worth disturbing her by treatment, and yet a few hours afterwards she was comfortable, and every alarming symptom had gone." Such recovery as this is only seen in these cases of pure sapræmia.

In the milder cases recovery, when it occurs, is usually rapid and complete; but in the more severe cases convalescence may be accompanied by great anæmia due to the destruction of the red corpuscles and hæmoglobin.

Morbid Anatomy. — The appearances found on post-mortem examination of these cases are very similiar to those occurring in animals in which the disease has been artificially produced. They are somewhat indefinite, and present nothing absolutely characteristic. Rigor mortis comes on early and soon passes off, being in most cases but slightly marked. Decomposition rapidly sets in, and even in cold weather putrefaction of the body prevents proper examination; the organs, eight or ten hours after death, are diffluent or distended with fœtid gases. The blood remains fluid for some time, and gravitates, causing marked hypostatic congestion. Coagulation occurs but slowly, and the clot formed is soft.

The lining membrane of the vessels and endocardium is blood stained, and there may be extravasations of dark blood beneath the skin, pleura, pericardium, in the brain, etc. Occasionally the pleura, pericardium, or other serous cavities contain a little blood stained fluid. The liver and kidneys are usually swollen; occasionally small hæmorrhages are seen in them, and microscopically the glandular cells are swollen and cloudy, or coarsely granular. The spleen is almost invariably much swollen, deeply congested, and occasionally almost diffluent. Various microbes which have been found in the tissues are almost certainly of post-mortem occurrence, and in a few hours they swarm in the body.

Diagnosis presents no difficulty in a ordinary case where we have the sudden onset of febrile symptoms in connection with an obvious cause. It may not at first be possible to say positively which form of septic disease is present, but the effect of treatment and the progress of the case will decide the question in a few hours. In doubtful cases of sapræmia and septicæmia the test of treatment must be relied on to exclude the former, the fact of importance being to determine if septicæmia be present.

It must also be remembered that certain symptoms of "collapse" or "shock," on or about the third day after operation, are commonly due to sapræmia. It is probable that large numbers of deaths after ovariotomy and other operations on the abdomen which have been ascribed to shock and exhaustion are really due to sapræmia.

As to **prognosis** but little need be added. In simple cases of sapræmia the prospect of recovery is always hopeful if treatment be immediately adopted, however bad the patient may appear at the time. In the old and debilitated, however, the prognosis must be regarded as much more serious. Also the risk of other septic troubles arising in connection with the same cause must be borne in mind, and this cannot be dismissed entirely until granulation is established.

Finally it may be said that recovery, when it occurs, is not only rapid but complete.

Treatment is mainly surgical, and needs but a brief allusion. The two main points to be aimed at have already been indicated, namely, to remove the source of the trouble as thoroughly as possible, and at the same time to injure the tissues as little as possible. The first point is attained by opening up the part freely, removing any decomposing

material found, and then flushing all the surfaces of the wound thoroughly with a mild antiseptic lotion. Thus if the cause of the trouble be blood-clot or pieces of placenta or membranes retained and decomposing in the uterus, the cervix must be dilated as far as necessary, the offending substances removed by flushing, or by the fingers, or by curetting as gently as possible, and then the whole uterine cavity thoroughly irrigated. If the cause be a wound of one of the large serous cavities this must be freely laid open, cleansed in a similar way, and means taken to ensure efficient drainage.

The second point is to handle the tissues as gently as possible, and to avoid the use of strong antiseptic solutions for flushing purposes. These solutions as applied only act mechanically by washing away decomposing material, and cannot destroy all the organisms present. On the other hand they act deleteriously on tissues already weakened by contact with the poisonous products, so that the wounds allow organisms to enter, to act on the parts more easily, and perhaps even cause their death — thus providing a fresh nidus for the putrefactive bacteria. Such fluids as sterilised water, boracic acid, or perchloride of mercury (1–6000 or 1 in 10,000) solutions are to be preferred. The best temperature at which to use them is probably about 100°–105° F., as this does not damage the tissues, and it acts as a general stimulant.

Afterwards the wound must be treated on general surgical principles. At the same time the condition of the patient must be carefully attended to. The cause being removed, rapid recovery will ensue if the effects of the poison already absorbed can be arrested. The collapse of severe cases must be treated by large quantities of stimulants frequently administered. Brandy must be given by mouth, or per rectum if vomiting persist; strychnine seems to be of special value. Carbonate of ammonia in two or three grain doses may be given hourly, or sal volatile in half-drachm doses. In very severe cases hypodermic injections of ether must be resorted to, and repeated as necessary; in a word, every effort must be made to keep the patient alive for a few hours until the poison in his blood is excreted.

In milder cases but little medical treatment is required beyond attending generally to the excretory functions. A diet consisting chiefly of milk with as much fluid as the patient cares to drink may be ordered, a large quantity of fluid serving to dilute the poison and hasten its excretion. If vomiting persist it may be allayed by a simple effervescing mixture, or by small doses of hydrocyanic acid and bismuth. As convalescence is established, a liberal diet with general tonics — iron, quinine, or strychnine — or perhaps change of air will be beneficial.

B. Septicæmia

The pathology of this disease is much more difficult than that of sapræmia, and indeed it has not as yet been definitely worked out: I do not know of any complete solution of it. From my description

of the experiments on animals, it would seem to be very simple, namely, that in sapræmia we have poisoning with the chemical products, in septicæmia we have a blood disease (the organisms growing in the blood), and in pyæmia we have in addition to blood disease the formation of secondary abscesses; but when we come to the pathology of these diseases as they occur in man, we find that it is not so simple as would appear from the investigations in animals. As a matter of fact, in cases grouped under the name septicæmia, we have not, as a rule, to do with a disease resembling the so-called septicæmia of the lower animals, in which the organisms are growing freely and in large numbers in the blood. True, on examining the blood taken from septicæmic patients, pyogenic cocci can usually be found; but they are generally in small numbers, are demonstrated with difficulty, and do not, as regards their numbers or distribution, in any way resemble the septicæmia of mice or rabbits: one is thus tempted to consider septicæmia after all as a chemical poison similar to sapræmia, the organisms producing this chemical poison not being in the circulating blood. In septicæmia, however, we have one marked difference from sapræmia. In the latter case, washing out the decomposing products from the wound, or removal of the part which is the seat of decomposition, at once arrests the disease; the explanation being, as before said, that the organisms producing the poisonous materials are growing outside the body, and that the poisonous materials are absorbed from the surface of the wound; on the other hand, it is evident that in septicæmia the manufactory of the poisonous products is not necessarily in the wound itself, but may be in other parts of the body — in other words, we have to do here with an infective disease caused by parasitic micro-organisms which are able to live in the body itself.

As to the place where these organisms live and produce their products, I believe, as I have just said, that but a slight effect is produced by the small numbers of organisms found in the circulating blood. The main body of them are at rest in the system, and from the parts where they are deposited they pour their poisons into the blood.

One of the common seats of these organisms is the tissues of the wound itself which, in an advanced case of septicæmia, would generally be found infiltrated with the cocci. Although they do not grow freely in the circulating blood, they get into it, and are carried by it and deposited in various parts; after death it is not uncommon to find in cases of septicæmia numerous capillaries throughout the body blocked with collections of cocci which have not yet led to abscesses. In these cases I believe the organisms have become adherent to the endothelium of the blood-vessels, and having succeeded in overcoming the resistance of these cells they grow there, and form the plug which is found after death.

A few cases where the symptoms are similar, though probably more acute, have been found to depend on the growth of organisms in large numbers in the blood — usually bacilli; this condition corresponds to

that found in the lower animals. The organisms which are usually associated with septicæmia are, however, the pyogenetic organisms, either the staphylococci, or perhaps more commonly streptococci. On post-mortem examination careful search generally shows a few organisms in the blood, and they may be cultivated from the blood of some of the internal organs — more especially of the kidneys, where they are sometimes in considerable numbers. In cases of bacillary septicæmia it seems that the plugs are not uncommon in the heart muscle. The organisms are always found in considerable numbers in the wound, in the pus, or discharges, in the membranous deposit which is sometimes seen on its surface, and deep in the neighbouring tissues; sometimes in the lymphatics and the neighbouring lymphatic glands.

It is difficult to understand how organisms like these pyogenetic cocci can at one time cause a simple abscess, and at another a severe and rapidly fatal general disease; apparently this depends on the variation and virulence of the organisms. These pyogenetic cocci increase in virulence when injected into the peritoneal cavity, and we find that inoculation from septic peritonitis is one of the commonest causes of the very rapid and fatal form of the disease in man. Apart from variation and virulence, the initial dose of the organisms which enters the body has a great deal to do with the result, while predisposition on the part of the body, and the existence of weak points where the organisms can settle and develop are also of great importance. It seems probable that under the term septicæmia several different septic diseases are grouped; but the possibility of making out the state of the case is becoming more and more difficult, owing to the spread of the principles of antiseptic surgery, and the consequent increasing rarity of the cases — at any rate in the hands of those who would be able to investigate their pathology.

The disease may arise from a simple prick or puncture inflicted during a dissection or post-mortem examination. In these cases the small size of the wound forbids all idea of poisoning by chemical products alone, and the disease which establishes itself is usually extremely rapid in its course, and accompanied by great fatality. Most commonly the disease follows wounds which have not been treated aseptically, and where, consequently, the pyogenetic organisms are present. Why it should arise in one individual with a septic wound and not in another is, as has already been said, not at all clear.

Apart from the virulence of the organisms and the condition of the patient, local conditions no doubt play a very important part, such as much bruising in the wounds, especially of the muscular tissues, in which the organisms can therefore readily settle; the muscles, moreover, are very plentifully provided with lymphatic vessels. Perhaps the most important local cause is the retention of the decomposing fluids in the wound leading to that amount of pressure which would help the entrance of the organisms into the blood or lymph stream.

In former times the contagious nature of the disease was well shown by the severe outbreaks which occurred from time to time in the surgical

wards of hospitals. The disease once introduced spread from patient to patient with great readiness; most probably being communicated by the surgeons or nurses, especially in the use of the same instruments for dressing successive cases without proper disinfection. More dreaded still was it in some of the large maternity hospitals, where there are records of many outbreaks, especially at the beginning of the century. In some cases half or two-thirds of the women delivered contracted the disease, and practically all of these died.

The post-mortem changes which are found in septicæmia (apart from the presence of deposits of organisms in various tissues or organs) are almost identical with those found in sapræmia. Rigor mortis is as little marked; putrefaction proceeds with the same extreme rapidity; there are the same blood changes, blood staining, serous effusions, etc. The spleen, however, is rarely quite so large, and congestion of the lungs and bronchitis are more or less constantly present.

Symptoms.—In discussing the symptoms, general and local, the severer and more typical form of the disease will first be treated, and subsequently reference made to the milder varieties.

General Symptoms.—The disease commences abruptly, often as early as a few hours after inoculation, usually within twenty-four hours. Accompanying the changes in the wound the temperature is observed to be rapidly rising; rigors occur in more than half the cases, and are usually repeated and severe. The temperature usually remains high throughout (103°–105° F.), with slight remissions. In the severer cases the patient's life is rapidly endangered; death may occur as early as the second or third day. The pulse is always very rapid, sometimes particularly feeble and irregular; the heart sounds weak. The respiration is rapid, there may be dyspnœa and cyanosis, accompanied by all the signs of catarrhal bronchitis. There is always complete anorexia, sometimes accompanied by vomiting, more rarely by diarrhœa.

The cerebral symptoms also vary much. There is usually headache more or less severe; in some cases delirium sets in early and is followed by coma,—more usually, perhaps, the mind remains clear to the end. If the case last longer the patient passes into a typhoid state. The skin usually assumes an icteric tint and purpuric spots may occur. The urine, besides the usual febrile characters, frequently contains albumin, and micrococci (in cases due to them) can usually be detected in it when freshly drawn off from the bladder. The gastro-intestinal symptoms become severe, and the patient dies from exhaustion usually within a week.

Although the differences in the symptoms noted above may possibly depend to some extent on corresponding differences in the causative agent, yet with our present state of knowledge it is impossible to say how far this is the case. No trustworthy observations on this point have yet been made.

The symptoms of the milder varieties of this disorder need only be alluded to: they are those which ordinarily occur in connection

with suppuration and septic wounds. There is always fever, but the temperature rarely reaches 104° F., and rigors are unusual. The patient feels ill, suffers from headache and thirst, the tongue is furred, and there is anorexia. Vomiting may occur, and constipation is the rule. In these cases also micrococci, if carefully searched for, may be found both in the blood and in the urine. As the state of the wound improves the fever subsides and the patient becomes convalescent.

Local Signs.—The changes at the site of inoculation or in the wound also vary greatly. In severe cases from a post-mortem prick the finger in a few hours becomes greatly swollen and intensely painful; thin red lines of inflamed lymphatic vessels may be seen spreading up the arm, and the axillary lymphatic glands become affected. Very shortly the whole arm may become swollen, œdematous and painful. In rare cases the disease is apparently arrested in the glands, and suppuration occurs there, and also along the course of the lymphatics. In these cases, the abscesses being freely opened, recovery may ensue; but more often the infection rapidly passes beyond them. Sometimes a form of gangrene spreads rapidly from the site of infection. In other cases no suppuration occurs, but the wound becomes covered with a yellowish white adherent membrane. In this membrane and in the serous flaky discharge bacteria can often be demonstrated. In other cases, again, no marked changes occur at the site of inoculation. In the milder cases the wound is usually in a more or less unhealthy state, suppurating and painful, with swollen reddened margins.

It is probable that some forms of hectic fever may be due to staphylococci growing in the granulations and the tissues bordering on the wound, and pouring their products into the blood stream. As these organisms are thus growing in the living tissues, according to our definitions as above, some forms of hectic fever must be considered as "chronic septicæmia."

The **diagnosis** may be made with ease and certainty if the case arise in connection with a small wound (an obvious source of infection), or if the wound present some characteristic state as above described. In other cases extreme difficulty may arise.

The distinction from sapræmia has already been pointed out; from pyæmia it can usually be made by its acuter onset, more rapid progress, more sustained temperature, and, later, by the absence of secondary abscesses. The possibility of a severe or malignant type of specific fever, such as small-pox, may also be borne in mind. The presence of streptococci in the blood and urine may be of help in some doubtful cases. The possibility of overlooking the severer underlying condition, and regarding the case as one of simple severe bronchitis with cardiac failure, must be guarded against. The milder cases with suppurating or septic wounds present no difficulty.

Prognosis in the severer forms, if an absolute diagnosis can be made, is almost hopeless. In extremely rare cases, as has been mentioned, the disease may be arrested in the lymphatics, and the patient ultimately

recover after a prolonged and severe illness, which often leaves him with an impaired constitution. Although persons in apparently robust health may be less liable to fall into the disease, yet when once established it is as fatal in them as in those of weaker constitutions.

Treatment. — On first seeing a case, the wound, if a small one, should be excised, and the parts freely cauterised with pure carbolic acid or the actual cautery. In cases of larger wounds thorough cleansing, followed by application of pure carbolic, may be carried out; or, if they be situated on an extremity, the question of immediate amputation must be considered. These measures, however, rarely do any good, the disease running its course unchecked.

The most that can be done is to support the patient's strength in every way, by administering in small, frequent quantities such nutriment as he can absorb, by giving stimulants — brandy and carbonate of ammonia — freely, and by combating in a suitable way some of the severer symptoms. Thus the temperature may be controlled by tepid sponging, vomiting by bismuth or alkalies, and narcotics may be given where there is pain. Of other drugs quinine is, perhaps, of as much use as any.

Pyæmia

When we consider the great interest in this disease, and the terrible mortality that it caused among surgical patients up to a recent period, it is very remarkable to find so few references to it in older works, and to note the little interest which it apparently excited among surgeons. Massa in 1559 and Ambrose Paré in 1561 pointed to the occurrence of abscesses in the lungs as the result of head injuries; but no precise theory to account for this was formulated until Boerhaave published his researches in 1720. Boerhaave affirmed that the complications of septic wounds were due to the admixture of the pus of the wound with the blood; and in spite of many adverse theories and criticisms this view received general support and maintained its ground until our own day. John Hunter, while apparently adhering to the view that pyæmia was due to the admixture of pus and blood, demonstrated the existence of suppurative phlebitis, and believed that the walls of the veins secreted the pus. The presence of suppurative phlebitis in almost all cases was also demonstrated by others, of whom we may mention Dance in 1828. In 1834 Gunther, and also Castelnau and Ducrest, injected considerable quantities of pus into the veins of dogs and cats, and succeeded in nearly every instance in producing metastatic abscesses. Virchow, in 1846 and later, pointed out that the material in the inflamed veins is not pus, but softened and altered blood-clot; and that it is cut off from the circulation by more recent blood-clot not yet broken down; and he held that the alleged mixture of blood and pus is really a leucocytosis. He strongly opposed the idea that pus enters the circulation from the veins or from the lymphatic vessels; in the latter case he pointed out that the glands must stop the corpuscles. In 1826 Cruveilhier drew attention to

the constant association of suppurative phlebitis with metastatic abscesses. He injected globules of mercury into the circulation of the lower animals, and noticed that abscesses formed where the globules lodged in the vessels; and he believed that pus from the veins lodges and acts in a similar manner. In 1842 D'Arcet stated that purulent infection consists of two parts which are quite distinct from each other, but always occur together, namely, poisoning by putrid products and a blockage of the vessels by emboli; the first leads to fever and general symptoms, and the second to the metastatic abscesses. This theory has been more or less accepted by Virchow and others. Virchow further separated septicæmia (which term he also applied to cases of septic poisoning) from pyæmia, and showed that the two might occur separately. Most of the experiments in support of this view were performed with putrid pus: the well-filtered solution, when injected into the veins, produced only septicæmia; the unfiltered solution containing solid particles led to pyæmia.

When the importance of bacteriology in connection with surgery was recognised these views were carried a stage further, and the causal agents were shown to be organisms growing in the decomposing pus. In 1867 Sir Joseph Lister first published the results which he had obtained by adopting the germ theory as the explanation of the occurrence of suppuration in septic diseases; and, acting thereon, the brilliant success of the antiseptic treatment soon fully confirmed his views, and, in spite of criticism, it has constantly gained greater and greater acceptance, till now it is fully recognised and firmly established. The view now generally held of the pathology of pyæmia is that the general symptoms are due to poisoning with the products of certain pyogenetic bacteria, and the abscesses for the most part to plugging of the blood-vessels with masses of these bacteria, or with emboli infected with them.

Pathology. — Many investigations have been made to determine the organisms which are associated with pyæmia, and it has been found that the organism usually present is the streptococcus pyogenes; though in some few instances, more especially in the less severe forms, pyogenetic staphylococci have been the only ones present. As I have said, the fever and general symptoms of pyæmia may be explained as those of septicæmia; that is to say, they are due to poisonous products poured into the blood stream by pyogenetic cocci growing in the living tissues of the body. The formation of the secondary abscesses is, however, not altogether quite easy to explain at first sight, for many observers have found pyogenetic cocci circulating in the blood of patients with septic wounds in whom no secondary abscesses were established. Ribbert and others have found that the injection of moderate quantities of staphylococcus pyogenes aureus into the circulation of rabbits is followed, as a rule, only by abscesses in the kidneys, the other organs apparently remaining unaffected; hence other conditions beside the mere presence of pyogenetic organisms circulating in the blood stream are found necessary for the production of the complete picture of pyæmia.

The almost constant presence in these cases of *suppurative phlebitis*

has already been mentioned; and there seems no doubt that the secondary abscesses — at any rate in the lungs — are explicable on the view that portions of the softened and infected thrombus become detached and form emboli in these organs. The sequence of events would then be as follows: — (1) Phlebitis occurs in direct connection with the wound; (2) a thrombus impregnated with micrococci is formed in the vein; (3) the thrombus softens, disintegrates, and portions of it are carried into the circulation as emboli; (4) these lodge in the first set of capillaries and form infarctions, and then abscesses.

In support of this view are the following experiments: — Ribbert, in experiments on rabbits with staphylococcus pyogenes aureus found that he could produce abscesses in the heart and in various organs if the cocci were injected into the blood stream attached to particles too gross to pass through the capillaries of these organs. He used a cultivation of the pyogenetic cocci on potatoes, and took care in removing the cultivation to scrape off also the superficial layer of the potato itself. If this mixture of potato granules and organisms was rubbed up with water, so as to form a fine emulsion, and then injected into the circulation, the result was the production of deposits of organisms in various parts of the body, leading to the formation of abscesses. Bonomé found that by mixing cultivations of pyogenetic organisms with finely powdered elder pith, and injecting the mixture into the jugular vein, he obtained similar appearances; but if the fragments of elder pith alone were employed no abscesses resulted.

Various other experiments might be quoted, but these and the pathological facts are sufficient to show that the ordinary pyogenetic cocci are able to cause secondary abscesses in the lungs if they enter the general circulation attached to gross particles, and to establish the importance of thrombosis and embolism as factors in the production of pyæmia. The point of difficulty, however, is to account for the abscesses in organs other than the lungs in cases where the systemic veins are affected; or than the liver in cases where the portal area is the seat of the primary disease. It seems hardly probable that fragments of blood-clot would be able to pass through the pulmonary capillaries and stick in the vessels of the kidney and other organs, and some other condition must be found to account for the presence of these farther abscesses.

It has already been mentioned, in speaking of the experiments on animals, that Koch found micrococci by means of which he could produce pyæmia; and that the way in which the deposits of organisms were brought about was by their growth in the blood, forming masses of organisms, and more especially entangling blood corpuscles. It is very probable that something similar takes place in man, and that the streptococci growing only in small numbers in the blood tend to form balls, which may be increased by the aggregation of blood corpuscles, and ultimately attain a size which cannot pass through the capillaries. It is possible, also, that in the lungs a fresh suppurative phlebitis may occur in the neighbourhood of the secondary abscesses, and thus lead to the

passage of emboli into the arterial circulation. While, however, some of the tertiary abscesses, as we may call them, may be brought about in this way, the view hardly suffices fully to explain the pathology, because it is found that these abscesses are more numerous in certain organs, more especially in the kidneys; whereas if plugs of cocci were floating about in the blood there seems no reason why they should be deposited more in one organ than in another. There appears, therefore, to be some selective power on the part of the organs, and such an admission clearly invalidates a pure embolic theory. It seems probable that most of these tertiary abscesses occur in this way — that the organisms floating in the blood, in groups not sufficiently large to form emboli, find conditions in certain organs more favourable to their deposit and growth than in others, and establish themselves in the endothelium of the blood-vessels, grow, and form plugs, and subsequently abscesses. Or again, it may be that they find a weak spot, caused by an injury or otherwise, in which they can settle; or again, there seems evidence in support of the view I put forward some years ago, which has since received a certain amount of confirmation, that apart from the rupture of blood-vessels and communication with the ducts of secreting organs there may be an actual secretion of the organisms. For example, in the case of the kidney, the organisms may pass from the blood with the water and get into the urinary tubules without any lesion of the wall of the blood-vessel or tubule; and having reached the tubules they may then find conditions, such as rest in a suitable soil, which enable them to develop, and there developing, may form masses and subsequently abscesses. I found distinct evidence of this some years ago in experiments on the lower animals with a certain coccus obtained from wounds, wherein, after injection into the blood stream, the kidneys were the only organs which showed signs of disease, and the organisms in the kidneys were present in the urinary tubules. This is the most probable explanation of the occasional occurrence of the abscesses in the parotid and other glands sometimes seen in pyæmia.

The suppurations in joints and serous membranes which occur in pyæmia are also probably brought about by a settlement of the organisms in the endothelial cells of the capillaries in these membranes, which grow there, and then pass into the joint or cavity and set up the infection.

From what has been said it seems, therefore, that the embolic theory of pyæmia must be extended, and that the occurrence of abscesses in various organs and in the joints must be farther explained by supposing either fresh formation of emboli in the circulating blood, or deposit of organisms in the endothelium of the smaller vessels and their growth there; or exit of organisms from the blood-vessels into the tissues in connection with injuries; or excretion of organisms and their growth in the tubules of the glands, or a combination of these. Various other factors no doubt come into play in the production of pyæmia, such as the dose of organisms, the degrees of their virulence, the general depression of the vitality of the body, and so on; but the above are the essential points.

We must now briefly trace *the changes which take place in the tissues* on the impaction of a septic embolus, or on the development of a mass of organisms in a small vessel or tubule, which changes result in the formation of an acute abscess. If we make a section through a commencing pyæmic abscess, and stain it appropriately, we shall find that in the centre, obviously in the lumen of a vessel, there is a small deeply stained mass which, under a high power of the microscope, is seen to consist of enormous numbers of cocci. Surrounding this is an unstained clear area in which the structure of the tissue is no longer readily discernible; this is an area which has undergone coagulation necrosis [*vide* articles on "Inflammation" and "Retrogressive Nutrition"] as the result of the action on it of the concentrated poisonous products poured out from the central mass of cocci. Outside this zone, where the poison is weaker, the tissues of the part are seen to be undergoing inflammatory changes; at a later period the micrococci burst through the wall of the vessel, and pass into the dead tissue, and even for a certain distance into the inflamed and living tissues; while from the outer part a large amount of fluid plasma and a large number of leucocytes are poured into this same dead area. Among the properties of these organisms is their power of peptonising albumin, and by virtue of this power the necrosed tissues are dissolved, while the effused plasma does not coagulate; thus a central fluid mass is formed, in which are floating large numbers of dead leucocytes and micrococci, and surrounding this mass we have a dense layer of newly-formed granulation tissue in which the pyogenetic cocci are present.

In man pyæmia may originate in connection with any inflammation in which the pyogenetic cocci are present; thus it may follow injuries and surgical operations where suppuration is allowed to take place, either from the use of imperfect precautions to ensure asepsis, or from conditions of the case preventing absolute asepsis. In former times this disease was the great dread of surgeons, and the cause of terrible mortality after all operations; but more especially did it follow injuries to veins, bones or joints. It was most often seen in hospitals, and especially in war, where the hygienic conditions were bad, and many wounded were crowded together. It is interesting to note that so late as the first decade of antiseptic surgery (1869–1878) there were no less than 903 cases of fatal septic disease, chiefly pyæmia, in eight of the large London hospitals.

Acute suppurative osteomyelitis, or periostitis, is a not unfrequent cause of pyæmia, the great tension under which the pus is formed probably forcing the septic emboli from the veins into the circulation. It is not so common after abscesses, boils and carbuncles; but, in the forms of suppuration, such as spreading cellulitis, due to streptococcus pyogenes, and in acute and chronic middle ear suppurations, pyæmia is not uncommon. It may also follow ulcers of the skin or of the intestinal tract; and in the latter cases the depressed general condition of the patient may promote the occurrence of the disease.

As to age, statistics point to pyæmia being more common between the years of 30 and 40; but this is probably due to accidental causes: no age

is exempt. Its frequency has also been found to vary with the seasons, being more common in damp and cold weather; probably because of the increased neglect of hygienic precautions prevailing at such periods.

Symptoms. — The ordinary form of pyæmia will be first considered, and later the distinctive features of the other varieties. The disease usually commences within the first week of an injury or operation. The wound generally becomes unhealthy, any granulations which have formed disappear, the previously sealed inter-muscular planes open up, and the discharge becomes thin, watery or sanious pus, often so scanty that the wound may appear dry. Phlebitis of the veins leading from the affected part may be made out, forming at first tense cords, accompanied later by surrounding thickening and tenderness; and, if superficial, by œdema and redness of the skin. In other cases, as in thrombosis of the lateral sinus, severe pain and tenderness along the course of the vessel may be the main local indication of phlebitis; or again we may have to draw an inference from œdema of the area drained by the vein. In rare cases the wound may appear healthy and even heal, and thrombosis, even if present, may be overlooked.

The general symptoms are usually ushered in by a severe rigor and a rapid rise of temperature to 104° or 105°. For a few days before this there will probably have been some general malaise and loss of appetite, accompanied by more or less fever. The rigor is followed by profuse sweating, and the temperature rapidly falls to 102° or 101°, or even lower. The rigors are usually repeated throughout the course of the disease; rarely are they absent for more than 24 hours at a time, although they occur quite irregularly, and two or more may occur in the course of a few hours, or even in connection with a single rise of temperature. The temperature is always high during the rigors — 104° F.–105° F.; even 110° F. has been certainly registered; in the intervals of the rigors it may be 100° F.–101° F., normal or even subnormal. The rigors are always followed by most profuse and exhausting sweats, and, together with the course of the temperature, are fairly characteristic; they may, however, occur with such daily regularity that the chart resembles that of a case of quotidian ague, or again the temperature may be more continuously high and rigors absent. Profuse sweating is in any case an almost constant symptom.

Usually there is anorexia and sometimes vomiting; but occasionally the appetite remains good until near the end, and the digestive functions may be but slightly affected in the earlier stages of the less severe cases. This may be accounted for by the periods of apyrexia or comparative apyrexia, which give the patient time to recover from the effects of the fever. In other cases there may be severe and frequent vomitings, or, more rarely, persistent diarrhœa. The tongue is usually furred, but cleans in the afebrile intervals; later, it becomes brown and dry, and the teeth and lips are covered with sordes. The breath is often said to have a sweet smell. Excessive thirst is common, and the patient will consume a large amount of fluid.

From the beginning the pulse is very rapid and soon becomes soft; later, it becomes very feeble, running, irregular or uncountable. The first sound of the heart is usually weakened, and may become almost inaudible. Various cardiac murmurs may also be heard; they are usually functional in origin, but in these cases the possibility of ulcerative endocarditis must always be borne in mind. Examination of the blood shows that the white corpuscles are increased in number, relatively and absolutely; and in some cases pyogenetic cocci have been seen in the blood, or obtained from it by cultivation. The respirations are increased in frequency; sometimes there is marked dyspnœa and cyanosis, but this usually occurs only in connection with some bronchial or pulmonary affection, of which, however, it may be almost the only clinical manifestation. The urine usually contains a small amount of albumin, but acute nephritis is very rare. The amount passed is usually about normal as a large amount of fluid is taken in the diet. The urea and urates are increased, and there is a diminution in the amount of inorganic salts. If blood and pus be present they point rather to a renal abscess. The patient rapidly loses muscular power, the muscles become flabby and waste rapidly, and all movements are very tremulous.

For a long time the patient's mental faculties are retained, or he may perhaps be delirious during the fever, and completely conscious during the intervals. Towards the end of the disease low muttering delirium is common, and the patient usually sinks into a comatose state. In other cases marked cerebral symptoms are present. Wild, noisy delirium and prolonged periods of unconsciousness are seen, and very severe headache is not uncommon. These symptoms are usually the result of the fever: cerebral abscess or meningitis cannot be recognised in the absence of direct localising symptoms.

The skin is often slightly tinged with yellow, but rarely much jaundiced, except in some cases of liver abscess. Occasionally an erythematous rash is seen much resembling scarlet fever in general appearance, but differing from it in its distribution; it chiefly occurs on the parts around the axillæ and groins, and spreading down the limbs, is rarely pronounced on the chest: more rarely still a pustular rash occurs. In the later stages of the disease petechiæ are not uncommon, or extensive cutaneous hæmorrhages may occur. Death usually ensues about the end of the first or during the second week; very few cases live more than three weeks. The patient may die of exhaustion, with all the symptoms of the typhoid state, and coma usually precedes death. Or the patient may die from the direct effects of a secondary lesion, such as cerebral abscess or meningitis, extensive pulmonary disease, heart affection, etc. In rare cases death occurs suddenly from impaction of a large embolus in the pulmonary artery.

The local symptoms, consisting of secondary abscesses in various organs and other parts of the body, and suppuration of the serous membranes, must now be considered. These usually appear about the sixth to the tenth day of the disease; and, in the ordinary form of pyæmia, the em-

boli originate in the systemic veins, and consequently are most usually arrested in the lungs. The lungs rarely escape secondary deposits in cases of pyæmia arising from disease of bones, such as osteomyelitis or periostitis from compound fractures, amputations, or other wounds involving bones; and in these cases the lungs only may be affected. In other cases, however, it is more usual to find abscesses in other parts with or without abscess of the lung; these arise either from the emboli being sufficiently minute to enable them to pass through the comparatively wide pulmonary capillaries, or from emboli formed in some of the other ways above discussed.

Many abscesses may form in the lungs and yet give rise to no very definite symptoms. The dyspnœa is increased and there are general signs of bronchitis. If an abscess form near the surface of the lung it will set up a localised pleurisy; then we have the characteristic pleuritic pain, cough, etc., and on auscultation the friction sound. Soon fluid is poured out into the pleura, at first commonly serous, but later becoming purulent; or the lung abscess may burst into the pleura. In either case a localised empyema is formed with or without pneumothorax, and may be recognised by the usual signs. Occasionally an abscess near the surface of the lung is sufficiently large to cause dulness on percussion and the other signs of consolidation.

Pleurisy may also occur apart from pulmonary abscess; and this has been more commonly noted in cases of pyæmia arising in connection with middle ear disease. The spleen, kidneys and brain are the other organs most commonly attacked in this form of the disease. In the spleen some pain and enlargement accompanied by great tenderness may be detected, and the abscesses bursting into the general peritoneal cavity may cause acute general peritonitis. Multiple abscesses in the kidneys usually give rise to some pain and tenderness with albuminuria; occasionally all symptoms are absent; or again there may be acute nephritis with pus and blood in the urine. The last symptoms are the only trustworthy ones on which to base a definite diagnosis, and they are but rarely seen. Abscesses in the brain and purulent meningitis can only be diagnosed definitely when some definite localising symptom is present; general symptoms, such as headache, vomiting, optic neuritis, coma and the rest, may occur apart from particular cerebral lesions. Abscesses in the liver also occur, especially it seems after head injuries. They arise in connection with the branches of the hepatic artery, and thus differ from those of portal pyæmia. The symptoms will be discussed later under this heading.

The eyes may also be affected in a very important manner: optic neuritis may occur with hæmorrhages scattered in the retina; the arteria centralis retinæ may be plugged by an embolus; this causes sudden blindness of the affected eye, followed by suppuration of the eyeball — panophthalmitis. The latter result will also follow if an embolus lodge in the ciliary region or iris.

Suppuration in the joints is one of the commonest lesions of pyæmia,

and may occur in any joint. There is usually intense pain at the onset, rapidly followed by purulent effusion, and then the pain often subsides more or less completely. The joint shows all the signs of acute suppurative arthritis, but if the affection be treated early by free evacuation of the pus, it is remarkable how little permanent damage may follow.

Suppuration in the peritoneal cavity also not uncommonly occurs; and may be primary, or secondary to an abscess of one of the viscera which may burst into it. It is very common in puerperal cases, in some probably due to direct extension. It is usually general, but may be localised at the outset. Pain at first is severe and accompanied by all the symptoms of acute peritonitis; later, however, pain and tenderness are often both absent; excessive tympanites from paralysis of the intestines is present; and, the purulent effusion being distributed throughout the abdomen, but nowhere in large quantity, dulness or fluctuation may never be obtainable. In this absence of signs the affection is commonly overlooked.

Purulent effusion in the pericardium may also occur, sometimes preceded by signs of pericarditis, friction sounds, etc., but often coming on very insidiously.

In the cellular tissue of the body large abscesses may form and burrow extensively. There is usually severe pain at the outset, but afterwards this may subside; the swelling is often very diffuse, and tenderness may not be very marked. Transient patches of œdema and redness of the skin and subcutaneous tissues, subsiding without suppuration, are also described (Erichsen). Abscesses in the muscles are very rare. In the heart they are also rare. The symptoms are indefinite, but the cardiac action is greatly impaired, and death is liable to occur from rupture of the heart wall. In rare cases abscesses are seen in the parotid gland, thyroid gland and testicles. Their possible pathology has been discussed.

Morbid Anatomy. — After what has already been said this may be dealt with very briefly. The general blood and tissue changes are exactly similar to those already described in septicæmia, but are usually somewhat less marked. They are the effect of the fever and general blood poisoning.

The wound will be found as already described; and if careful search be made, a thrombosed vein will often be found leading from it. Such veins are filled with soft adherent clot, in some places breaking down, in others replaced by pus, which is always shut off by clot from the general circulation. Around the vein there is a certain amount of periphlebitis, or even a periphlebitic abscess. Cases have also been seen (six cases, *Path. Soc. Reports*) in which thrombosis followed by embolism has occurred in a vein remote from the seat of infection.

In the lungs signs of bronchitis and broncho-pneumonia are almost constantly found. Hæmorrhagic infarctions are rarely seen, but scattered throughout are abscesses varying in size from a pea upwards. In the kidneys and spleen also the abscesses are commonly multiple. In the brain it is not uncommon to find a large area of acute softening, the result of an embolus, with only a drop or so of pus in its centre. Pyogenic

organisms of one or more varieties can be demonstrated in large numbers in the original site of infection, in the emboli and thrombosed veins, and in the secondary abscesses; but rarely in the blood.

Suppurative Pylephlebitis or Portal Pyæmia. — This form of pyæmia is extremely rare. The commoner causes of it are suppurative appendicitis, ulceration of the intestine, especially dysentery, malignant ulceration of stomach or intestines, chronic gastric ulcer, and ulcerative diseases of the rectum. Suppuration of the gall-bladder, ulceration from gall-stones, or suppurating hydatid cysts, may also cause it. Cases of a foreign body which has been swallowed and has penetrated to a branch of the portal vein are on record; and we have already mentioned cases in the newly born following phlebitis of the umbilical vein.

The result of the suppurative phlebitis of the portal system is the production of pyæmia similar in all its general symptoms and pathology to that already described, but differing from it in that the chief secondary deposits occur in the liver. Numerous abscesses are always seen throughout the liver, obviously arising in connection with branches of the portal vein. The liver is uniformly enlarged — sometimes very large — the capsule may be normal or covered with patches of peritonitis, and the abscesses may show on the surface. The clotting may occur throughout the portal vein, and even spread through into the hepatic vein. These abscesses must be distinguished from those arising from gall-stones and the like, where the infection spreads up directly by means of the bile ducts; from abscesses in ordinary pyæmia, which arise in connection with the hepatic artery, and are usually fewer in number; and also from the large tropical abscesses. In none of these is portal thrombosis present, and the mode of origin is usually obvious.

Only the special symptoms due to the implication of the liver will here be referred to. The disease is always of a severe type, and runs a rapidly fatal course. There is intense pain in the right hypochondrium, and the liver rapidly enlarges. It is very tender on palpation, with an ill-defined, soft margin. Signs of gastro-intestinal irritation, especially vomiting, are common. Two characteristic symptoms are ascites and marked jaundice, but they are by no means constant. Ascites occurs when a considerable extent of the portal vein is blocked, but it may also be due to peritonitis. Jaundice occurs when a large bile duct is pressed on or involved in an abscess, but there is always some bile passed in the fæces.

The diagnosis may be completed by placing the patient under an anæsthetic, and thoroughly using a large exploring needle or trocar, but even then an abscess may be missed.

General peritonitis may be caused by rupture of an abscess into the peritoneal cavity. The spleen is always much enlarged.

So-called Chronic Pyæmia or Multiple Abscesses. — This disease arising under similar conditions to true pyæmia, and leading to the formation of secondary abscesses, has long been confounded with pyæmia. It differs, however, essentially from true pyæmia in that embolism apparently plays no part in it. Pyogenic organisms reach the blood stream by a wound,

or the like, and, owing to the depressed vitality of the patient, continue to live there, but produce only slight disturbance. Then if some spot be weakened by the result of a slight injury, the organisms fix on that spot, develop in it, and produce an abscess. The injury producing the abscess is usually slight, such as a strain, too long or too great pressure on a part, and so forth. The abscesses are consequently few in number, often only one or two, and are situated in the subcutaneous tissues or in the joints. The disease may last for months, the general symptoms not being severe; elevation of temperature, pain, etc., occur at the commencement of each fresh abscess, but subside in the intervals.

A case is recorded in the Pathological Society's *Transactions*, in which a compound fracture of the lower jaw was followed by suppuration occurring at the site of other fractures sustained at the same time. The fracture of the femur was noticed suppurating nearly a month after the injury, and ten days later the fractures of the humerus and rib were affected. Numerous experiments on animals have shown that the simple injection of small numbers of pyogenic cocci into the blood stream will be followed by no ill effects, but that if simultaneously an injury be inflicted on any part of the body a local abscess will result.

Diagnosis of Pyæmia. — Difficulties mainly arise in cases where the source of infection is unusual or obscure; it must also be borne in mind that a patient with a suppurating wound may contract a fever, such as typhoid. In all suspected cases such sources of infection as osteomyelitis, chronic middle ear suppuration, ulcerative endocarditis, suppuration in the nose or in connection with carious teeth, ulceration of the mouth, throat, or alimentary tract, rectal diseases, gonorrhœa, and so forth, must be very carefully inquired into.

Of the diseases more or less resembling pyæmia typhoid fever is the most important; indeed, pyæmia has been called wound-typhoid. In both we find a similar temperature, and in both an enlarged spleen; similar abdominal symptoms may also be present; in both the typhoid state supervenes, and there may be an absence of other definite symptoms. To distinguish typhoid we must inquire into a possible source of infection; the rose-coloured rash and peculiar stools are decisive; hæmorrhage from the bowel is extremely suggestive; the abdominal symptoms may be prominent, and the fever is usually more regular. Moreover, in very rare cases pyæmic infection may arise in connection with the typhoid ulcer. On the other hand pyæmia is indicated by the discovery of a probable source of infection, by the irregular course of the temperature, by the recurrent rigors and profuse sweating, by petechiæ in the skin, by optic neuritis and retinal hæmorrhages, and, lastly and conclusively, by the formation of multiple abscesses.

Typhus fever, now extremely rare, also closely simulates pyæmia. The abrupt onset, high fever, and cerebral symptoms, are common to both. The diagnosis between them must rest on the mulberry rash of typhus, or on the secondary abscesses in pyæmia. In acute tuberculosis the temperature may be similar, and there may be no decisive symptoms.

We must look for other signs of a tubercular disease and a tubercular history. Later, the slower onset of the disease, its protracted course, signs of tubercle in the choroid, and the absence of local signs of abscess, show the true nature of the disease.

Pyæmia may closely simulate malaria in the course of the fever and sweatings. The history of exposure to malarial influences, or previous attacks of it, the absence of local abscesses, and above all the effect of quinine, will decide the question. Acute rheumatism and pyæmia have in common a similar course of temperature, profuse sweats, inflammation of serous membranes and joints, and perhaps endocarditis. In acute rheumatism the sweat has a very peculiar sour odour; the inflammation of the joints often subsides suddenly and attacks other joints, and there is no jaundice or sign of embolism.

With regard to ulcerative endocarditis it must be remembered that the murmur varies much and may be absent, and that the disease is most common after pneumonia.

The differences between the rash of scarlet fever and a skin affection sometimes seen in pyæmia have already been pointed out, and these diseases have few other symptoms in common.

The diagnosis from septicæmia is not important, and rests entirely on the presence of secondary abscesses.

Pyæmia may have to be distinguished from meningitis when head symptoms are very prominent, or from uræmia in cases of acute nephritis.

In the **prognosis** of pyæmia the varieties of the disease must be separately noticed. Cases of ulcerative endocarditis and suppurative pylephlebitis are invariably fatal.

In ordinary surgical pyæmia the prognosis is very grave and recovery extremely rare. The majority of the patients die in the first week, and very few survive more than two weeks. The worst cases are those associated with high continuous fever, extreme vital depression, and the early formation of visceral abscesses. In the cases which recover, as a rule only external abscesses have occurred; and even then an impaired constitution, stiff joints and tendons usually remain. In cases of chronic pyæmia, on the other hand, recovery is not infrequent, but after months of suffering and with the deformities above mentioned.

Treatment. — The preventive treatment may first be considered. This is purely surgical, and consists in the thorough adoption of the antiseptic methods wherever possible. In other cases every precaution, and especially free drainage, must be adopted to keep the wound as healthy as possible. At the same time the patient's general health must be carefully attended to, a good supply of fresh air provided, and overcrowding especially of patients suffering from suppurating wounds, must be avoided. Even where thrombosis of a vein has occurred in connection with suppuration the pyæmia may be cut short by freely opening up, purifying, and draining the source of infection, and at the same time cutting off from the circulation and cleansing, or, much better, excising the whole of the thrombosed vein.

The disease once established nothing but symptomatic treatment can be attempted. The fever, if very high or continuous, may be controlled by antipyretics, or better still by such means as tepid sponging. Quinine in five grain doses two or three times a day may also be tried. Cardiac failure must be mainly combated by stimulants, of which brandy or whisky are the best, and these may be given in large quantities. If vomiting be present champagne may be tried. Severe vomiting may be allayed with bismuth or small doses of hydrocyanic acid. Morphia is required in many cases to relieve pain. The patient's general health must be supported by abundance of such light nourishment as he can digest; and an unlimited quantity of fluid, such as barley water, "imperial drink," milk, and soda-water may be allowed. Special care must be taken in the nursing to avoid bed-sores. Secondary abscesses must be promptly opened and drained.

W. Watson Cheyne.

ERYSIPELAS

Definition. — A contagious disease characterised by a peculiar spreading inflammation of the skin, or more rarely of a mucous membrane, due to a specific micro-organism, and associated with general febrile symptoms.

The contagious nature of the disease was not recognised until about 1850, and apparently first in England. Later Velpeau pointed out this fact in France, and showed, as Trousseau had previously done, the frequency of its origin in connection with a wound or abrasion. In Germany Wernher in 1862 adopted these views, and Volkmann in 1869. This contagious nature has now been conclusively proved, and that the disease originates almost invariably in connection with slight wounds or abrasions is generally admitted; but there is even yet much dispute as to the exact limits of the name. The older authors applied it to a large number of distinct skin affections (such as eczema, etc.), and also to diffuse phlegmonous inflammations of internal organs and serous membranes. The skin affection known as erysipelas is now sharply distinguished, and the name is not applied to internal inflammations; though some authors, following Nunneley (1841), still describe as erysipelas spreading diffuse forms of inflammation affecting the subcutaneous tissues with or without associated skin affection, and even such diseases as whitlow.

It has also been held that erysipelas can give rise by contagion to pyæmia, puerperal fever, and other septic diseases, and vice versa. There is, however, no sufficient evidence in favour of these views, and the statistics of a report to the Pathological Society of London tend to disprove any connection between them.

It seems more in accordance with the present state of our knowledge to regard inflammation of the subcutaneous cellular tissue as a distinct (although a closely allied) affection due to a separate cause; and when the two affections occur simultaneously and run concurrently, to regard the disease as due to a mixed infection. This subject must be further considered when the specificity of the causative micro-organism is discussed. A distinction has also been drawn between surgical erysipelas, or that complicating wounds, and medical erysipelas, which latter mainly attacks the face and is supposed to arise idiopathically. Usually, however, it arises in connection with some slight injury of surface, and there is no essential difference in the two diseases. Although typically a skin affection and limited to the cutis vera, the disease may attack mucous membranes, either spreading to them by direct extension from the skin, or, originating on a mucous membrane such as that of the throat, it may spread to the skin, or possibly even remain limited to the mucous surfaces.

Etiology. — The causes of this affection may be either general or local, some perhaps act both generally and locally. The disease is widely spread, and usually occurs in an endemic form; rarely distinct epidemics of it have been noted. Women are more liable to it than men, and people between the ages of 35 and 55 are chiefly attacked. *Season* seems to exert a decided influence on its prevalence, the disease being most common in spring and autumn, much less so in summer and winter. February and November are the months in which the disease is more especially prevalent, — months, that is, usually associated with considerable changes of temperature, but on the whole cold and damp. This may be in part accounted for by the overcrowding in unhealthy, ill-ventilated rooms, and the want of proper exercise, which commonly occur at such seasons.

Erysipelas formerly was not uncommon in the surgical wards of hospitals, and especially in those which were ill ventilated or defective in sanitary arrangements. In these wards, if once introduced, the disease was extremely difficult to eradicate, and nearly every patient with a wound would be attacked, the *contagion* being probably conveyed by the hands of the dressers, etc. Where the hygienic arrangements are good, and efficient means are taken to prevent direct conveyance of the contagion by the hands or instruments, the disease shows but little tendency to spread; the poison is never widely diffused through the air. It clings closely, however, to furniture, bedding, clothes and the like, and may be conveyed by a third person. The disease is not uncommon in patients debilitated by recent acute diseases such as typhoid fever; and in general it is more common among the poor and weakly, whether from improper food, bad hygiene, or the exhaustive effects of chronic disease, especially perhaps of albuminuria and diabetes.

Certain persons show a marked disposition to the disease, and suffer from many attacks of it throughout their lives: the attacks sometimes show a kind of regularity, returning every spring or sometimes even more often, and this disposition has been said to be hereditary. It may be in part a general disposition, but many cases may possibly be explained by

the constant presence of a chronic disease producing a weak spot or slight abrasion from which the disease originates; in favour of this view it is found that the same spot is attacked time after time. Thus such persons may be found to suffer from an irritating discharge from the nose or ears which excoriates the surrounding skin. It is probable that one attack confers *immunity* for a very short time; it has been found impossible to inoculate successfully a patient who had had an attack five weeks previously; a second attack, however, may occur after three or four months.

The most important predisposing condition is *a wound*, which may be of any size; the smallest abrasion, by removing the epidermis, seems sufficient to allow the organisms to gain a foothold. This advantage may be given not only by trauma, but by irritating discharges from ozæna, otorrhœa, or even a common cold; or by chronic eczema, lupus, and the like. It has frequently been asserted that a small wound, such as one of these, is invariably the starting-point of the disease, and that, as Volkmann says, erysipelas is a true traumatic infective disease. This view is most probably correct, for if very careful search be made, some wound or abrasion will be found in the large majority of cases; for the others it must be remembered that the wound may have healed during the incubation period of the disease, and that if the disease be not seen at its commencement, the swelling, etc., that occurs will soon mask it. The fact that the disease on the face generally starts at the margins of skin and mucous membranes, or near the external auditory meatus, where excoriations are so common and so easily overlooked, lends much support to this view. In searching for wounds it may be remembered also, as Fehleisen has shown, that the disease may first appear at some little distance (3 cm.) from the point of inoculation.

The immediate cause has been most conclusively shown by Fehleisen to be a streptococcus very closely allied to, if not identical with the *streptococcus pyogenes*. Micrococci of various kinds had been previously recognised in the blood and lymphatic vessels of the skin of the affected part, chiefly at and just beyond the spreading margin of the disease, by such observers as Lukomsky, Von Recklinghausen, Koch and Billroth. They also described the cocci as occurring in the subcutaneous tissues and in the internal organs; indeed, there is a great probability that most of their observations were made on cases of erysipelas complicated with cellulitis or pyæmia. Fehleisen was the first to describe accurately and to isolate a specific streptococcus, to cultivate it in pure cultivations outside the body, and to demonstrate its direct causal relationship with the disease.

On examining *sections of skin* taken through the margin of the spreading redness, he observed numerous micrococci growing in chains in the lymphatic vessels and spaces of the corium, not in the blood-vessels as other observers had stated; these he found to be most numerous at and just beyond the spreading margin of the disease, but in parts where the redness is passing or has passed off, the lymphatic vessels and spaces become infiltrated with leucocytes and the cocci rapidly die out. A few

cocci were also seen in the neighbouring subcutaneous tissues; the appearances were the same in all of thirteen cases examined. Pure cultivations were obtained on various nutrient media, — blood serum, jellies, and on potatoes. Fehleisen asserts that their growth in these media is characteristic, but most observers have failed to detect any difference between this growth and that of streptococcus pyogenes.

Experiments were made by *inoculating* the ears of *rabbits* with pure cultivations. A definite disease followed, characterised, as in man, by a sharp spreading margin of redness without suppuration. On making sections of the spreading margin the cocci were found in the lymphatic vessels and spaces presenting the same appearances as in man. Other organisms may, however, produce similar results in rabbits. But, further, Fehleisen, by *inoculating persons* the subjects of incurable tumour with pure cultivations of the cocci, has absolutely proved that these organisms are the cause of erysipelas in man. Of seven individuals so inoculated, six presented the disease in every way typical; the seventh case failed even after repeated inoculation, but he had suffered two or three months previously from an attack of erysipelas, and was probably immune. It was shown in some of the other six cases that immunity was conferred for at least a short time, as repeated inoculations failed to reproduce the disease. The method he employed was to make superficial scarifications over the part, and then to rub in the pure culture. The incubation period in these cases varied from fifteen to sixty-one hours, and it is also noted that the disease did not always start exactly at the punctures, a fact which has also been noted in cases occurring spontaneously.

It had long been noted that various malignant diseases — especially sarcoma and such chronic skin diseases as lupus and chronic eczema — were markedly improved or even cured by an attack of erysipelas; and many observers had endeavoured with more or less success to set up in such cases a *curative erysipelas*. It was for this reason that Fehleisen's experiments, which at first sight might appear unjustifiable, were undertaken; considerable benefit occurred in most of the cases, although probably none were cured. This treatment, almost abandoned because of its danger, has lately been revived in an improved form for the cure of some forms of malignant disease, the toxins of erysipelas obtained by sterilising a pure cultivation of the cocci being employed as a hypodermic injection.

An important question has been raised by a number of observers, who have asserted, and many still assert, that the *streptococcus of erysipelas* is identical with the *streptococcus pyogenes*, and that the different results depend on differences in other conditions, such as variation in the virulence, dose, seat of inoculation, susceptibility of the host, and so forth. Fehleisen asserted that in cultivations under similar conditions there were marked differences in the modes of growth of the two forms, and also that the inoculations in rabbits gave rise to similar but distinctive processes. Other observers, however, have totally failed to confirm these results. There is no doubt that the two organisms are very closely

allied species, but that they are absolutely identical seems difficult to reconcile with clinical experience in man. On the one hand, there is no sufficient evidence to show that the erysipelas cocci can cause suppuration in man — this result has never followed experimental inoculation with pure cultivations — and, on the other hand, inoculation into the skin of *streptococcus pyogenes* has produced suppuration, but not erysipelas. Thus, in opening abscesses which not infrequently contain streptococci, the skin is necessarily inoculated; and in one definite case (Rosenbach) a dense inflammatory induration appeared round the incision, but erysipelas has never been shown to result in such cases. The balance of evidence, therefore, seems to be in favour of the specific nature of the erysipelas coccus, but the point is still under discussion.

Some further experiments illustrating the mode in which the disease is spread may be alluded to. It has been found extremely difficult to transmit the disease directly from patient to patient, and prepared plates exposed to the air of wards containing cases of erysipelas have very rarely yielded cultures of the organism. They have been most successful when the patients were freely *desquamating*, when the scales thrown off have been shown by cultivation to contain living organisms. Thus it is probable that these scales are the most usual means of carrying the disease.

Pathology. — The minute anatomy of the local lesion has already been described, and as it will be further discussed under the symptomatology, but little need be said in this place. The redness of the skin disappears after death, but some of the swelling remains; blebs and effusion into the lax subcutaneous tissue are also seen. These blebs usually contain serum more or less turbid; they rarely contain organisms. The loose tissues of the eyelids, larynx, etc., may also be seen distended with serum, and the tension of the effusion may have been so great as to cause gangrene of these parts.

In patients dying of erysipelas, besides those dying of laryngeal stenosis, the characteristic appearances of the more fatal complications will also usually be found. Thus in many cases diffuse *cellulitis* will be seen, and often a resulting *pyæmia*. Disease of the kidneys must also be looked for. In such cases organisms are commonly found in the internal organs, but this is probably not so in simple cases of erysipelas. *Pneumonia or bronchitis* may also be found, more rarely *meningitis;* the latter has been said to arise from the inflammation passing directly inwards from the scalp to the meninges, or from the face along the trunks of the fifth nerve, but it is more probably a pyæmic symptom. If a person die of simple uncomplicated erysipelas, the internal organs simply show the usual signs of a septic disease or those common to the *typhoid state*, namely, swollen congested spleen, enlarged liver, and kidneys with cloudy degeneration of the glandular epithelium, etc.

Symptoms. — The incubation period of erysipelas has been variously estimated at from three to seven days. We have already seen that it is fifteen to sixty-one hours when the disease is experimentally produced.

The general symptoms commence somewhat abruptly, simultaneously with, or just before or after the appearance of the local lesion. The temperature rises rapidly; there is often a more or less severe rigor, the patient feels ill, is languid, and often has intense headache, anorexia or even vomiting. The fever and constitutional disturbance are usually in direct proportion to the extent of the local lesion. Herpes labialis is not uncommonly seen, and, apart from cases of erysipelas of the fauces, there is soreness of the throat accompanied by general congestion. The fever, with varying remissions, usually remains high while the skin affection is spreading, and often terminates suddenly with the cessation of the spread. The skin is hot and dry, but sweating occurs during the remissions of the temperature. Other febrile symptoms, such as rapid pulse, frequent respirations, febrile condition of urine, are also present, usually in direct proportion to the degree of the fever. In some cases after apparent cessation of the symptoms a *recrudescence of the disease* takes place, a fresh rise of temperature, etc., accompanying a fresh local outbreak. In the chronic cases of *wandering erysipelas* the temperature takes a very irregular course; it may become normal while the disease is still spreading, but usually a fresh spread is accompanied by marked but brief constitutional disturbances.

In the milder uncomplicated cases the general disturbance may be and usually is very slight; in other cases, more especially in debilitated constitutions, the gravest symptoms may supervene. The severity of the fever and its duration may bring on the typhoid state, and the patient sink of exhaustion. In other cases severe *gastro-intestinal disturbances* may be present — complete anorexia, obstinate vomiting accompanied by constipation or profuse diarrhœa — and these symptoms persist and exhaust the patient. Of albuminuria I shall speak later. In other cases, again, and especially in drunkards, *nervous symptoms*, such as intense headache and great restlessness accompanied by violent delirium, may be very prominent from the commencement. The delirium may pass into the low muttering type as the patient sinks into stupor, coma, and death. In most of the severer cases the *spleen* may be made out somewhat enlarged, and the skin is more or less jaundiced.

Locally, the disease as it attacks the face and head will be alone described. A sharply-defined patch of redness appears on the cheeks — or more usually at the junction of the mucous membrane of the nose and skin — at the margins of the lips, near the external auditory meatus, or near the margin of the hairy scalp. The affected portion of skin becomes red, hot, swollen and shiny, and is accompanied by a feeling of tension or burning pain; the patch spreads by direct continuity to surrounding parts. Extension usually occurs unequally in different directions, and the disease is very apt to be arrested by a fold in the skin or at the margin of the scalp. Where it is spreading there is always a sharply-defined, raised red line, separating the healthy from the affected tissues, which may be both seen and felt. Behind this line the redness and swelling gradually shade off until the parts become normal again.

The disease lasts in a particular spot about four or five days, so that it may still be spreading in another place while the part first attacked has become normal. Where the disease spreads over loose tissues much serous effusion oozes into them; thus the eyelids become enormously swollen, and the eyes are closed, the ears are greatly thickened, the wrinkles of the face obliterated, and the features quite unrecognisable. Blebs more or less large may also appear on the skin in the severer cases and add to the deformity. They contain serum, often turbid, or a sticky gelatinous fluid, and soon burst and dry up, leaving adherent crusts. Very rarely local gangrene may occur from the intense virulence of the inflammation and the tension of the effusion in such tissues as the eyelids, ears, etc. In such cases the eye may be destroyed. The glands in the neck are always enlarged and tender.

Definite *abscesses* occurring in the skin or subcutaneous cellular tissue are most probably the result of a mixed infection, and this is not unlikely to be the case when they occur, as is not very uncommon, in the eyelids.

When the disease spreads to *the scalp* there is usually increased headache accompanied by much local tenderness and œdema, but without redness. The disease may spread from the face to the neck and body. In some cases it assumes a chronic form, spreading from place to place until nearly the whole body has been attacked, and one part may even be affected twice. These cases are more common in children; the constitutional disturbance varies, but, as a rule, is mild, and recovery may take place after many weeks; in infants, however, recovery may be incomplete, and death occur later from marasmus. In these cases also the spreading margin of the disease is no longer distinct, but diffuse patches appear, often not in continuity.

Where the disease spreads over a joint, effusion takes place into its cavity. This is serous, perhaps turbid, but probably in simple erysipelas never purulent. Wherever the skin has been attacked considerable desquamation follows, and this, as has already been shown, is the chief means of dissemination of the disease.

I have already said that the various *mucous membranes* may also be attacked by erysipelas; the frequency with which this occurs varies in different epidemics. The disease may begin on the skin and spread by direct continuity to the mucous membranes of the nose, mouth, etc., or conversely; or, beginning at the junction of skin and mucous membrane, may extend simultaneously in both directions. There is also good reason to believe that some of the cases described as acute œdematous laryngitis and pharyngitis are really examples of erysipelas limited to that region. The disease always spreads from the throat to the skin, or vice versa, by direct continuity; and cases have been described which illustrate the four paths by which this extension may take place. In order of frequency they may be enumerated as follows: (1) from the lips by the mucous membrane of the mouth, tongue, etc.; (2) by means of the nostrils, nasal mucous membrane, etc.; (3) by the Eustachian tube and auditory

canal; (4) from the eyes by the lachrymal canal to the nose, etc. The mouth, ear, nose, tongue, palate, pharynx, larynx and trachea may all be affected. Cornil records eighteen cases in which the throat was attacked; in nine of these the affection spread inwards from the skin, in seven it originated in the throat. In the former case the throat was generally attacked on the third to the fifth day of the disease. In all these cases the general symptoms are much more severe, and gastro-intestinal disturbances are common. The throat is extremely painful, preventing sleep, and causing great pain and difficulty in swallowing. When the larynx is attacked there is the further danger of suffocation from laryngeal stenosis; or the disease may spread down the trachea, and broncho-pneumonia may be set up.

The local appearances on the palate and fauces are most characteristic. The whole part is uniformly dark, shiny, red, and feels dry and burning hot. Much œdematous swelling also occurs, especially affecting the uvula; the tonsils share in the process, but are not nearly so enlarged as in quinsies, and sometimes the sharp spreading margin of the disease may be distinctly seen. Bullæ, small or large, are frequently seen; at first they are well formed and contain turbid serum, but in a few hours they burst, leaving yellowish white, membranous-looking patches which persist some days. After the disease has subsided dilated veins are observed on the part.

When the nose is attacked the swelling of the mucous membrane entirely occludes it. In the mouth erysipelas gives rise to marked purplish red swelling and profuse ptyalism. In all these cases the glands at the angles of the jaw are markedly swollen and tender, causing great pain and difficulty in mastication.

When the larynx is attacked there is deep red congestion and swelling of the whole mucous membrane, and great œdema, especially affecting the epiglottis, aryepiglottic folds, and arytenoids. This œdema always comes on very suddenly, and may rapidly destroy the patient's life unless urgent means of treatment be adopted. In rare cases the inflammation goes on to gangrene: this usually attacks the œdematous parts, or arises in the membranous patches above described. All the symptoms are then aggravated, there is intense prostration, the breath is extremely fœtid, and septic forms of bronchitis and pneumonia may set in.

Two other forms of the disease may be briefly mentioned. In infants the disease may start in connection with *the navel*, and, though commonly fatal from the feeble resisting power of the patient, it presents no other peculiarity. Also in infants or young children the disease is not uncommonly seen to start from the *vulva*. Intense swelling and œdema of these parts occurs, with pain and great difficulty in micturition; not very uncommonly it results in gangrene.

Complications and Sequelæ. — The most serious local complication of erysipelas is diffuse cellulitis; this it is which gives rise to local suppuration, to pleurisy, pericarditis, meningitis, and the other pyæmic symptoms usually described as complications of erysipelas. Apart from septic in-

fection, pneumonia and bronchitis are occasionally seen, especially if the throat be affected.

Albuminuria is very commonly present as a symptom of erysipelas, and acute nephritis is not very rare. In drunkards delirium tremens may arise. Still more rarely by implication of the conjunctiva, the nutrition of the cornea may suffer, leading to sloughing and destruction of the eye; if the disease spread along the ear and Eustachian tube acute suppuration of the middle ear with all its evils necessarily ensues.

Among sequelæ may be noted increased liability to the disease after a brief period of immunity; and repeated attacks not uncommonly leave a greatly thickened, unsightly condition of the skin. When the scalp is attacked there is usually a falling off of the hair, which, however, soon grows again, unless the attacks be repeated. Chronic skin diseases — eczema, lupus, etc. — are often much reduced or even cured by an attack of erysipelas; in many cases after single attacks it has been noticed that the skin is finer and softer, and the complexion much improved.

The **diagnosis** of erysipelas of the skin is usually quite easy; the abrupt raised margin of redness, spreading by direct extension, and accompanied by constitutional disturbance, is characteristic.

Diffuse cellulitis is accompanied by more brawny swelling, and the superjacent redness of the skin is more diffuse. The redness accompanying lymphangitis is also more diffused, and, at least in parts, the thin red lines of the larger inflamed vessels may be made out.

Erythema of the skin occurs in bright red diffuse patches, and spreads by the formation of fresh distinct patches. It chiefly resembles the migratory form of erysipelas, but is not accompanied by pain or any constitutional disturbance.

Acute eczema spreads by the formation of tiny, pin-point lesions, usually minute vesicles; it has a weeping surface, and never anywhere a distinct raised margin. Other skin affections — such as herpes, pemphigus and urticaria — need scarcely be mentioned.

In the throat, also, erysipelas presents characteristic points apart from its general association with skin affection. The pharynx is more acutely painful, the constitutional disturbance greater, the local signs of swelling and œdema more marked, and the parts of a deeper red than in simple acute pharyngitis. The tonsils are not nearly so large or inflamed as in quinsy. Herpes of the palate is not associated with so much general congestion or swelling, and the constitutional disturbance is slight. When the larynx is attacked reliance must chiefly be placed on the accompanying severe bodily prostration to distinguish it from other forms of acute œdema. Scarlet fever may simulate both the throat and skin affection; but the scarlet rash never appears first on the face and is more diffuse and punctiform both on the skin and throat. The pultaceous throat sometimes met with in scarlet fever may, however, be indistinguishable from that following the formation of vesicles in erysipelas; the diagnosis must then be made by the concomitant symptoms.

The **prognosis** of erysipelas, as it occurs in healthy adults, is very

favourable; but some epidemics are much more severe than others. Mild cases last two or three days; the severer ones five to ten days: the migrating form may last for weeks, and in any case after apparent cessation relapses may occur.

Erysipelas attacking surgical or puerperal patients is apparently much more fatal than the kind above described; but the mortality formerly occurring in such cases was probably due in part to the lowering treatment (bleeding, and so forth) too often adopted in patients already depressed; and in part to other complications of the wound. The disease is more fatal in the aged; and in infants it tends to assume the spreading form which not unfrequently leads to marasmus and death.

In patients suffering from chronic renal disease the prognosis is extremely bad; it is also grave in the subjects of chronic alcoholism or of any wasting disease such as diabetes, phthisis, malignant disease, chronic suppuration, and the like.

Cases in which the throat is attacked are more dangerous than those in which the skin is affected alone; and those cases in which the disease spreads inwards from the skin are said to be much more dangerous than those in which the extension takes places in the opposite direction. When the larynx is involved the case becomes extremely grave, apart from the special danger of suffocation. Gangrene of the throat is almost necessarily fatal.

In most cases the severity of the general disturbance, the pulse, temperature, gastric and mental symptoms will give trustworthy data on which to base a prognosis.

Treatment. — The disease being contagious the patient must be isolated as soon as possible; especially must he be kept away from all communication with patients suffering from wounds, and from puerperal cases. The attendants on the sick must also be very careful of any cuts, cracks or abrasions on their hands, and these attendants must not at the same time look after other patients, especially not those suffering from wounds. If these precautions be rigidly carried out, and other cases treated aseptically, there is little harm in the patient remaining in the same ward with them. On recovery the patient's bed, clothes, and other articles must be thoroughly purified, and the walls and furniture around well washed. During convalescence, when desquamation is in progress, increased care must be taken; if the patient's skin be affected it should be well greased with vaseline or olive oil, or, if the area be small, with carbolic oil (1–40), and the part sponged with a weak solution of permanganate of potash many times a day until the process has come to an end.

In the ordinary milder cases seen in adults no active medicinal treatment is required. A light, nutritious diet, with possibly a little stimulant, is prescribed; the action of the bowels should be attended to in conjunction with some of the local means of treatment about to be described, and the disease will get well of itself.

In severer cases more active treatment is required, and, the disease

being essentially adynamic, no lowering methods must be adopted. The diet must be chiefly fluid, milk, eggs and the like, with a liberal allowance of stimulants. If vomiting be present it may be met by effervescing mixtures or bismuth, and the regular action of the bowels must be ensured. The worst cases require a very large amount of stimulants; and carbonate of ammonia and strychnine may be prescribed in addition. Should the temperature remain persistently high, or hyperpyrexia be present, the effect of large doses of quinine may be tried; but as a rule tepid sponging or the cold bath will prove a more efficient method of treatment. Other antipyretics are less to be trusted, and have too great a tendency to depress the patient. For great restlessness, want of sleep or delirium, sponging may be employed, or an ice-bag applied to the head. If these fail morphia is probably the best drug to use, or bromides with chloral may be given.

In addition to the above symptomatic treatment two drugs may be mentioned, which at different times have been considered to act almost as specifics. Of these the best known is perchloride of iron, which is given in very large doses (℥ 40–60 of the tincture) every four hours. This drug is certainly well tolerated in these cases, and by maintaining the patient's strength probably does good in many. The other drug is camphor, recommended by Strümpel, but is of more doubtful value. Camphor is given in three grain doses every two or three hours, and at the same time the patient is encouraged to drink large quantities of hot tea, so that he soon perspires freely. Quinine was also at one time considered a specific.

Numerous methods of local treatment have been recommended at various times, the very number showing their general inefficiency. It is probable that the simplest are the best; such are dusting the affected part with powdered boracic acid, zinc oxide, or a mixture of these with starch, and covering the part with a thin layer of cotton wool. This in part relieves the painful local sensations, is cleanly, and does no harm. For the face, it is a good plan to cut a mask of lint with holes for the mouth, nose, and eyes, and to keep this moist with evaporating lead lotion. This is very soothing, but must never be applied to any part where there is the least tendency to gangrene. Where the pain is great tinct. opii (2½ oz. to the pint) may be added to the lotion. These two methods are better than simply dusting the part thickly with flour, or applying plain water dressings. The dry powders are also much better than the various pastes which are sometimes recommended, and better than the ointments, at least at this stage. Painting the affected part with collodion usually does harm. If there be very great tension in the affected part, or gangrene threaten, free incisions must be made into it at once, and antiseptic fomentations applied.

Formerly it was much the fashion to apply nitrate of silver over the healthy skin — just beyond the spreading margin of the erysipelatous redness — care being taken not to destroy the whole thickness of the skin; it was asserted that in a considerable number of cases the erysipelas came

to a standstill when it reached the line so made. Unfortunately, however, it very often crosses at some part or other and spreads on as before. In place of nitrate of silver some surgeons use iodine. At first sight the value of this method of treatment is not very obvious, and many have asserted that in the cases where the disease was arrested at this line they had to do with mere coincidence. From recent work on the pathology of the disease, however, we can see that the plan was not so foolish as may appear. As previously mentioned, the erysipelas cocci spread in the lymphatic vessels of the skin, and it has been found that while, on the one hand, when we have to do with an acute, rapidly-spreading erysipelas there is very little cellular infiltration in the part, yet on the other hand, when the process is mild, or when it is coming to a standstill, a large number of cells are found forming a barrier against its further progress. Now the application of nitrate of silver to the skin in so strong a solution as to cause slight ulceration will lead to a rapid exudation of leucocytes which may fill up and block the lymphatic vessels of the part; and thus when the cocci in their spread reach that line, they may find their path barred by a collection of leucocytes.

Not very long ago, when the parasitic nature of the disease was first understood, attempts were made to arrest its spread by the injection of weak antiseptic solutions — such as 2 per cent carbolic acid solution, weak perchloride of mercury lotion, etc. — into the healthy skin just beyond the spreading margin. This method proved untrustworthy. More recently, however, it has been improved by Krause, whose method of treatment is highly spoken of by those who have experience in erysipelas. This plan is to make numerous scarifications in the healthy skin beyond the spreading margin, the scarifications crossing one another and completely surrounding the disease, as did the old nitrate of silver line. In order to carry out this plan efficiently the patient must be placed under an anæsthetic. When the scarification is complete, a steam spray-producer, containing 1 to 20 carbolic acid, is made to play on the part for some considerable time (an hour or two); it is subsequently dressed with carbolic compresses. I cannot speak personally of this method, as my experience in the treatment of erysipelas is insufficient.

When the mouth is affected it should be constantly washed out with simple gargles of boracic acid, Condy's fluid, or sanitas; and if the nose be attacked it should be gently syringed with similar solutions. When the throat is attacked the gravity of the affection must be borne in mind, and in spite of opposition on the part of the patient, a considerable amount of fluid nourishment and stimulants must be administered. The pain of swallowing may be considerably mitigated by the simple plan recommended by Mr. Hovell: an attendant standing behind the patient makes firm pressure during the act of deglutition over the ears and part of the neck below by the palms of the hands, the fingers being directed upwards. Locally the patient may be directed to suck ice constantly, and to use weak antiseptic gargles frequently. Sometimes, on the other hand, frequent gargling with a hot saturated solution of bicarbonate

of sodium will give most relief, and at the same time hot fomentations may be applied around the angles of the jaw. If these measures fail, free scarification of the palate, and especially of the uvula, will always afford relief. When the larynx is attacked the special danger of suffocation is added, and treatment must be mainly directed to prevent this. All food must be given cold, and all hot or steam inhalations scrupulously avoided. Formerly great reliance was placed on leeches, six to twelve being applied over the larynx, and they certainly give temporary relief. But their tendency is to exhaust the resources of the patient, and usually they have to be repeated. Other means of counter-irritation are useless. The best plan of all is to keep the patient constantly sucking ice; at the same time he should keep quite quiet, and avoid all use of the voice. In some cases this treatment will be all that is required. Where, however, in spite of this the swelling increases, we must either perform tracheotomy or freely scarify the larynx. The effect of the latter may be first tried in adults, where the patient is not too intolerant of the necessary manipulations, and where the dyspnœa is not so extreme as to render the method dangerous from the reflex spasm it excites. The method recommended is as follows: —cocaine is not used, its application wearies the patient, excites spasm, and does no good — guided by the laryngoscope a long, deep incision is made into each ary-epiglottic fold, most efficiently by an open knife like Heryng's, rather than by a guarded instrument like Mackenzie's scarifier; it is better to make the incisions into the outer side of these folds, so that the blood may have less tendency to trickle into the larynx, and thus to cause much discomfort or even serious danger to the patient. The bleeding is promoted by gargling with hot fluids, and afterwards the patient continues to suck ice.

If this fail to relieve the dyspnœa tracheotomy will be required, and this should be done as soon as its necessity is foreseen, so as to give the patient his best chance of recovery. Where scarification is out of the question, as in children and adults who cannot tolerate the necessary manipulations, tracheotomy offers the sole hope of relief; for all other methods of scarifying — by the finger nail, or by a guarded bistoury guided by the finger touch — are to be strongly condemned as unscientific and dangerous.

When the parts around the vulva or anus are attacked much relief may be obtained by immersing the child's body in a warm bath to which small quantities of tincture of iodine may be added. The child is swung in a sheet and properly supported, and may be allowed to remain in the bath twenty-four to forty-eight hours at a time.

Finally, in addition to the general and local treatment above described, the presence of complications must be carefully sought or watched for, and especially must the state of the kidneys be investigated, and appropriate treatment adopted in the respective cases.

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INFECTIVE ENDOCARDITIS

Synonyms.—Ulcerative Endocarditis, Malignant Endocarditis, Arterial Pyæmia, Mycosis Endocardii.

For some time two forms of acute endocarditis have been distinguished—the simple, benign or verrucose, and the malignant or ulcerative endocarditis. There now is abundant evidence that in both forms of acute endocarditis micro-organisms are formed; and though in some cases the same organisms have been found in the two forms, yet as the malignant type very frequently implants itself on the chronic form of benign endocarditis, and produces a new and often fatal train of symptoms, it is desirable that the two affections, so different in their character and principle features, should be considered separately.

Various names have been suggested for the malignant type, none of which, however, is quite unobjectionable: ulcerative and malignant endocarditis are those now most frequently used. Against the name ulcerative endocarditis it may be urged that occasionally no distinct ulcerations are found; whilst on the other hand the ulceration which may result from

degenerative changes in chronic endocarditis or in the arterio-sclerotic form — the so-called atheromatous ulceration — is not associated with the symptoms of malignant endocarditis. Against the name malignant endocarditis it may be urged that some cases recover; and again, that even the verrucose form may sometimes run a rapid and fatal course (29).

Infectious or infective endocarditis (E. infectieuse, E. infectante, E. végétante of French authors) is perhaps the least objectionable name, but as yet it has not been generally adopted by English writers.

As there is now clear proof that the cause of malignant endocarditis is a microbe, and as in many cases the organisms occurring in septic and pyæmic diseases have been found in it, we think that the proper place for infective endocarditis is amongst the septic diseases; in deference, however, to habit and convenience we propose to consider now only the etiology and general pathology of this form of endocarditis: the symptomatology, morbid anatomy, diagnosis and treatment will be dealt with in one of the articles on diseases of the heart.

History and Etiology of the Disease. — Bouillaud (1824–1832) is said to have been the first to indicate a form of acute endocarditis which occasionally began with pyæmic symptoms; but he did not recognise the relation of the endocardial lesions to the general symptoms: Stenhouse Kirkes was the first to comprehend the malignant form of endocarditis; he looked upon the general or typhoid symptoms as due to an altered condition of the blood produced by the granular masses detached from the diseased valves. Virchow not only pointed out the embolic nature of the blocks found in the small arteries in cases of valvular lesions of the heart, but, in a case of puerperal perimetritis, with peritonitis and diphtheritic deposits in the large intestines, he also described coagula with granular masses, like diphtheritic deposits on the mitral valve; and he looked upon the process as possibly due to a parasitic cause.

The pyæmic character of malignant endocarditis was also early noted by Dr. Wilks who afterwards suggested the name of arterial pyæmia for this affection (52); he was followed by J. W. Ogle, Murchison, Moxon, Bristowe, and other English writers. Bamberger and Friedreich laid stress on the similarity of the symptoms in some forms of endocarditis and in pyæmia; and of the early French observers we may note Charcot and Vulpian and Lancereaux, who described the clinical characters of malignant endocarditis. Not a few observers, such as Hayem and Dugues, and Desplats, looked upon the valvular lesions and the lesions in the other organs as local manifestations of a general infectious disease.

Winge was the first to describe microbes (which he spoke of as chains of small rods or round granules like chains of leptothrix) both on the valves and in the secondary infarcts in a case of infective endocarditis; and, as the patient had suffered from suppuration of a toe, he thought the microbes, which he regarded as the cause of the disease, were derived from this source: he accordingly proposed for the disease the name mycosis endocardii.

Heiberg found microbes similar in character to those seen by Winge in a case of infective endocarditis in a puerperal case. He inserted particles from the affected valves into the peritoneal cavity of a rabbit, but with negative results.

Nevertheless Heiberg's observations formed the starting-point of a series of similar publications all of which made for the existence of microbes in the diseased valves: some of the cases, like that of R. Meier, were primary infective endocarditis; in others (Wedel (50)), the primary source was septic endometritis, whilst in others again (27), the primary disease was pneumonia with empyæma.

Birch-Hirschfeld not only found numerous micrococci, in zooglœa masses and in chains, in the diseased valves and in the metastatic infarcts, but he also succeeded in producing panophthalmitis in three rabbits by inoculation with fragments from the valve deposit. Klebs made some important contributions to this subject: from an examination of twenty-seven cases of endocarditis he came to the conclusion that all forms of this malady are of mycotic nature; the verrucose form being due to cocci (monadines), the other (which he calls the septic endocarditis) to a somewhat different organism (a capsulated coccus). Koester, by a series of observations, confirmed the opinion of Klebs that every endocarditis, whether malignant or benign, is caused by microbes; finding, moreover, that many of the vessels of the affected valves were filled with thrombi consisting of cocci, he came to the conclusion that the endocarditis was produced by these microbic emboli which rupture the walls of the vessel and reach the free surface of the valve. About this time Cayley, who suggested the name infecting endocarditis (6), and Purcer published malignant cases of endocarditis in which they described the presence of microbes. Litten confirmed the observations of Klebs and Koester. In the meantime the clinical features of infective endocarditis, and its relation to the simple or rheumatic endocarditis, were made the subject of further study by many pathologists and clinicians, some of whom will be referred to in the clinical section; at present I will mention only the papers by Goodhart (17) and Osler (37).

With the progress of bacteriology, our knowledge of the organisms found in this disease has become more definite; pure cultures of them have been obtained, and their behaviour when injected into animals definitely followed. A series of important observations were published between the years 1885 and 1888, amongst others by the following observers: — Wyssokowisch, Cornil and Babes (9), Ribbert, Senger, Bramwell, Netter (35), Prudden, E. Fränkel and Saenger, Stern and Hirschler, Weichselbaum, Dreschfeld, O. Rosenbach. Of the papers treating on the etiology of this disease published since 1888 I may cite those of F. Taylor, Gilbert and Lion, G. Lion, Roux and Josseraut, and Dessy.

If we summarise the results of these and some other observations we arrive at the following data: —

1. That in nearly all the cases of infective endocarditis, whether ulcerative or not, microbes were found.

2. That in most cases only one organism was found, but in a few (Weichselbaum, Stern, Hirschler, Fränkel, etc.) more than one.

3. That the organism found was not the same in all. In many cases an organism was found which occurs in other infectious diseases, whilst in some an organism occurred not hitherto found in other diseases.

The organisms belonging to the first group were: the streptococcus pyogenes (including the streptococcus of erysipelas); the staphylococcus pyogenes aureus, the staphylococcus pyogenes albus; the pneumococcus of Fränkel and the pneumobacillus of Friedlander; the typhoid bacillus (16); the bacillus of tuberculosis (25, 8, 20); the bacillus of diphtheria (21); the gonococcus (29).

The organisms belonging to the second group were bacillus endocarditis griseus (Weichselbaum and Netter); micrococcus endocarditis rugatus (Weichselbaum); bacillus endocarditis capsulatus (Weichselbaum); bacillus immobilis et fœtidus (Fränkel and Sänger), and the bacillus of Gilbert and Lion (besides a few others with less definite specific characters).

4. In most cases the microbe found in the diseased valves was also met with in such secondary deposits as infarcts and metastatic abscesses.

5. The organisms most frequently found were the streptococcus pyogenes, the staphylococcus pyogenes aureus, and the pneumococcus. The first two were found chiefly in cases in which the endocarditis was primary, in cases of puerperal diseases, of pyæmia and septicæmia (wounds, abscesses, osteo-myelitis, etc.), and especially in those cases in which the infective endocarditis had attacked valves already affected with chronic rheumatic endocarditis.

The pneumococcus has been found mostly in cases where croupous pneumonia was present, and in some of meningitis without pneumonia. As streptococci and staphylococci have also been found in the diseased valves when the primary disease was enteric fever, diphtheria, gonorrhœa, and so forth, it is evident that sometimes the endocarditis is due to a mixed infection.

6. Experimental investigations on animals have led to diverse results. Particles of the diseased valves inserted into the subcutaneous tissue, into the peritoneal cavity, or into the anterior chamber of the eye, have sometimes produced no effect; but often they have given rise to local abscesses. Injections of pure cultivations into the peritoneum or under the skin sometimes produced no results; at other times they gave rise to marked septic symptoms and lesions.

Endocarditic lesions have been produced by the injection into animals (rabbits and dogs have most frequently been used for this purpose) of pure cultivations of the organisms found on the diseased valves in cases of malignant endocarditis. Some observers — Ribbert, Perret and Rodet, Bonomé, Dreschfeld, Mannaberg, Gilbert and Lion, Roux and Josseraut, and Vaillard — by injecting pure cultivations into the jugular vein of rabbits, succeeded, without previously injuring the valves, in producing inflammatory changes with or without ulcerations in the aortic valves, and often also on the mitral and tricuspid valves; and in

the valvular deposits masses of the organisms of the pure culture were found both on the surface, in the deeper layers of the deposits, and, in some few cases also, inside the capillaries and small arteries of the inflamed valves. Other changes found in the animals experimented upon were: — Enlargement of the spleen, metastatic infarcts, and hæmorrhage into the brain. These various lesions, though evidently the result of the microbes, were, however, by no means uniformly found. Gilbert and Lion, by the injection of a peculiar bacillus found in a case of infective endocarditis into a vein of the ear in rabbits, produced marked endocarditis with many secondary changes (softening and hæmorrhages in the central nervous system).

The majority of experimenters, however (Rosenbach, Orth, Fränkel and Saenger, Weichselbaum, etc.), only succeeded in producing endocarditis by injuring the aortic valves shortly before injecting the cultures into the jugular vein. The aortic valves were injured by introducing a sterilised stylet through the carotid into the left ventricle, a method first made use of by Rosenbach (43). Secondary or metastatic deposits of microbic origin were also found in these animals, together with other changes such as enlargement of the spleen, fibrinous deposits in the pleura, etc.

7. The examination during life of the blood of persons suffering from infective endocarditis has shown in a few cases, especially on the application of certain methods which will be given in the clinical section, the presence of microbes of the septic kind.

As regards the nature of infective endocarditis the conclusions which we may draw from the above data are: —

(i.) Infective endocarditis is a disease due to micro-organisms.

(ii.) This disease is not produced by one specific microbe only; other organisms, separately or together, may give rise to it.

(iii.) The organisms which most frequently are the cause of the disease belong to the septic and pyogenetic type (streptococci and staphylococci.

(iv.) Of other organisms, the diplococcus of pneumonia often gives rise to infective endocarditis; the specific organisms of enteric fever, gonorrhœa, diphtheria, tuberculosis do so very rarely: infective endocarditis occurring in the course of any one of these affections, or found in valves already the seat of chronic endocarditis or atheroma, is due to septic organisms, and must be looked upon as a mixed infection complicating these diseases.

(v.) The organisms more readily attack valves weakened or altered by disease.

(vi.) Some of the microbes found in infective endocarditis are also found in the rheumatic or verrucose endocarditis.

Etiologically we may distinguish the following types of infective endocarditis: —

(*a*) Primary infective endocarditis.

(*b*) Infective endocarditis as a complication of septic disease (pyæmia, septicæmia, puerperal affections, traumatism).

(*c*) Infective endocarditis as a complication of pneumonia or meningitis, and due to the diplococcus pneumoniæ.

(*d*) Infective endocarditis as a mixed infection due to septic organisms secondary to acute infectious fevers, or secondary to rheumatic endocarditis or sclerotic conditions of the valves.

Remote Causes. — 1. A debilitated state of the system. Though infective endocarditis occasionally attacks persons of sound constitution and in good health, it is more often noticed in debilitated persons, in drunkards, in persons suffering from nervous depression and the like, or suffering from such chronic exhaustive diseases as cirrhosis of the liver (45*a*).

2. The presence of an infectious disease. This point I need scarcely dwell upon again. Besides the various affections, septic and non-septic, already mentioned, we may note also dysentery, malaria, small-pox, scarlet fever, epidemic influenza (Fiessinger) as diseases which, by lessening the resistance of the body, favour the entrance and growth of the septic organisms. Syphilis does not appear to enter into the causation, and the endocarditis accompanying it is more of a sclerotic and fibrous nature with fibrous deposits in the myocardium.

3. During pregnancy and the puerperal state infective endocarditis has repeatedly been observed, especially in the presence of a septic or pyæmic affection of the uterus or its appendages.

4. Acute rheumatic arthritis, though much more commonly associated with rheumatic or verrucose endocarditis, occasionally gives rise to malignant endocarditis. Dr. Ogle recorded three cases, and others have been mentioned by Osler, Peter, Burkart, Fernet.

5. Chronic valvular affection of the heart, the result of chronic endocarditis or produced by sclerotic changes, commonly enters into the causation. Of sixty-nine cases of infective endocarditis, Dr. Coupland noticed sixty-one in which the valves had been previously affected, and Osler states that in three-fourths of his cases sclerotic changes persisted in the valves. (To avoid repetition, I will give the results of my own analysis when, in a later article, I consider the clinical aspects of this form of endocarditis.)

6. Gallstones, with or without suppuration in the biliary passages, have occasionally been known to give rise to infective endocarditis. As yet seven cases only have been published, but I may mention another which occurred in a patient under the care of my colleague Dr. Steell. Murchison had already noticed this association in his work on *Diseases of the Liver*. Other cases have been described by Jaccoud, by Mathieu and Malibran, by Netter and Martha, and more recently by Leva, who gives the literature on this subject. Netter and Martha (36) found a small bacillus in the biliary abscesses, and also in the endocarditic deposits. As the bacterium coli commune is occasionally found in calculous affections of the biliary apparatus, the connection between cholelithiasis and infective endocarditis, even when there is no suppuration, is easily understood.

7. That chorea, which is so closely connected with rheumatic endo-

carditis, may be associated with infective endocarditis, is shown by the following case which came under my care about two years ago. A boy, aged 11, was taken into the Manchester Infirmary suffering from chorea; there was no history of rheumatism, and, on admission, there were no signs of endocarditis. A week after admission he began to be feverish, and a loud mitral systolic bruit appeared; a fortnight later he showed signs of a cerebral affection (severe headache, delirium, optic neuritis, hemiparesis). At the post-mortem examination infective ulcerative endocarditis of recent date, and a small abscess of the brain with suppurative meningitis, were found. The valves showed no signs of chronic disease.

Barkley (39) gives a case of chorea, terminating fatally, in which endocarditis, abscess of the parotid, and broncho-pneumonia were found; the endocarditis in this case may possibly have been secondary to the pneumonia.

8. Traumatism, apart from external wounds and injuries, may give rise to infective endocarditis in another way, namely, by an injury causing rupture of a heart valve. Biggs gives a case in which the aortic valves were ruptured by a fall, and infective endocarditis supervened. A similar and very interesting case came under my notice. A gentleman, a patient of Dr. Stott of Haslingden, had been under observation for several years on account of slight albuminuria, for which he periodically consulted Sir William Roberts. He met with a severe bodily strain, and shortly afterwards, not feeling well, consulted Sir William Roberts again, who then for the first time detected a loud aortic diastolic bruit. He returned to Haslingden and, some short time after whilst out shooting in the month of September, he began to suffer from symptoms of malignant endocarditis (repeated rigors, which recurred almost daily, intermittent pyrexia in which the temperature rose to 105° F., and eventually embolism of the posterior tibial artery): from this state after a time he recovered. He is now in the enjoyment of good health, though the loud diastolic aortic bruit is still present.

9. Climatic conditions appear to me to have some influence in this matter. I have noticed that cases of infective endocarditis occur more frequently during the autumn; and in several cases the patient before the attack had spent some time in a swampy or marshy district. Decaying vegetable matter may have something to do with the outbreak of the disease in these cases.

10. Infective endocarditis occurs especially between the ages of 20 and 40. It is very rare in older people, and, according to Osler, it is also very rare in children (3 to 4 out of 209 collected cases). From my own observations infective endocarditis in children would appear not to be so rare as this estimate would indicate. Men are more frequently affected than women.

The paths of entrance of the microbes, as in other septic diseases, vary in the different groups of cases. We may notice as the chief portals: —

(*a*) The skin and subcutaneous tissue. Many of the septic cases,

following abrasion or ulceration of the skin, belong to this group; and likewise the cases of infective endocarditis following furuncles, carbuncles, gangrene, erysipelas, and the like. Considering how slight an abrasion may sometimes be followed by septic infection, it is possible that in some cases of the so-called "primary" infective endocarditis the germs may have entered the system in this way.

(*b*) The osseous system, as in osteomyelitis and otitis media.

(*c*) The mucous membranes of the digestive tract. Ulceration of the intestines explains the occurrence of septic endocarditis after enteric fever and dysentery. In several of the recorded cases, besides the ulceration in the intestines, there was an old lesion of the valves. Gangrenous stomatitis and ulcers on the tongue and lip are occasionally quoted (Brissaud, Gilbert) as primary channels of entrance. Probably the tonsils, which are so often affected in rhuematic endocarditis, may occasionally serve as the means of entrance, and thus again some of the so-called "primary cases" may be explained.

(*d*) Of the biliary passages we have already spoken.

(*e*) The genito-urinary organs. The frequent occurrence of infective endocarditis in puerperal disease and after abortions has been noted; the channels along which the infection travels are the uterine lymphatics and veins. In men the mucous membrane of the urinary tract may form the starting-point, as in gonorrhœa, or bladder and kidney affections, which have sometimes been followed by infective endocarditis.

(*f*) Respiratory tract. We know that many infective germs may pass into the blood through the respiratory passages, often after having caused such changes in the epithelium as facilitate their entrance into the blood. But it may also be admitted that germs may pass through the lungs, and find their way into the circulation without any previous injury.

The frequent association of infective endocarditis with pneumonia need scarcely be mentioned again: the disease has also been noted in bronchiectasis by Thiroloix. The microbes, having reached the blood, find access to the valves (where they produce more or less extensive lesions to be described hereafter under the pathological anatomy of the disease) either on their free surface by deposition from the circulating blood — a view first set forth by Virchow — or by way of the vessels of the valves in which they form small emboli, and thence penetrate into the tissue and to the surface — a view already attributed to Köster. Most observers are inclined to adopt Virchow's opinion, one strongly supported by experimental pathology (seeing that infective endocarditis so often attacks valves already diseased), and by arguments based upon the paucity of blood-vessels and capillaries in the valves even when inflamed. On studying the distribution of the micro-organisms in sections of the diseased valves, I have been struck by the gradual diminution in their number from the surface of the valve inwards; but this may well be due to the more favourable conditions on the surface of the valve for their growth.

Several observers, however (Cornil and Babes, Köster and others),

have described numerous emboli, consisting almost entirely of microbes in the vessels of the inflamed valves. There is no reason why we should not accept both views of the processes.

Chemical Pathology. — On this subject, which is sure to become an important one in all bacteriological diseases, we have to record the observations of Sidney Martin, who, in connection with his important researches on diphtheria, studied also the action of the chemical poisons in malignant endocarditis and in anthrax. A chemical examination of the blood and of the spleen (by his method) from a case of infective endocarditis, in which a staphylococcus, which could be cultivated, was found in the diseased valves, showed the presence of two bodies — a proteid (proto- and deutero-albumose) and a non-proteid product of strong acid reaction. The albumoses when injected into animals produced fever, and retarded the coagulation of the blood; and the fever increased with the quantity injected: the albumoses from anthrax were more toxic, and caused greater loss of weight in the animal. The post-mortem examination of the animals that died, or were killed, showed that no pathogenetic organism was present; when a large single dose of the albumoses was injected into the animal fatty degeneration of the heart was found after death.

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J. D.

PUERPERAL SEPTIC DISEASE[1]

History. — Before the comparatively recent recognition of the influence of infective germs in the causation of puerperal septic disease, the views entertained of the nature of this terrible scourge of obstetric practice were most chaotic and puzzling. Of course the frequency of the disease in practice had ensured attention to the subject from the earliest times, and explanations were almost endless; generally some prominent symptom was supposed alone to indicate the origin of the malady. For instance, Hippocrates, Galen, and many of the older authors, who distinctly recognised the disease, supposed it to be caused by suppression of the lochia, — an opinion which was maintained by many later obstetricians, such as Smellie, Denman and others. In France the view of Puzos that the disease was due to milk metastasis was generally accepted. This opinion was obviously derived from a mistaken theory of the nature of the peritoneal exudations so frequently observed after death. Similar errors prevailed in this country, where the disease was attributed to local inflammation; thus one attributed it to peritonitis, another to metroperitonitis, to metritis, or to inflammation of the veins and lymphatics. Other authors contended that puerperal fever was an acute specific fever, occurring in lying-in women only; this view was stoutly maintained by Fordyce Barker in his well-known work on *The Puerperal Diseases.*

It is not surprising that in the face of such various and contradictory views our knowledge of this fatal malady was narrow and unsatisfactory. Various observers, however, from time to time came to have inklings of the true nature of the disease, although these truths are now

[1] It seemed well to include this short article in the *System of Medicine*, as the general physician has often to treat cases of puerperal septicæmia. — ED.

only recognised in the light of our recent knowledge. The analogy of the interior of the uterus after delivery to the stump of an amputated limb (first pointed out by Harvey, and subsequently insisted upon by Van Swieten, Cruveilhier and others) was an approach at least to a recognition of the identity in this respect of a puerperal and a surgical patient, which is the essential fact in the interpretation of septic disease in childbirth; but the still more important lesions of continuity about the cervix, vagina and vulva, through which the absorption of the infectious materials so readily occurs, were not then noted. Some, however, suggested that the disease was due to the introduction of animal poisons into the system after delivery, and a subsequent vitiation of the blood; as, for example, Kirkland, who in 1774 wrote, "It sometimes happens that coagulated blood lodges in the uterus after delivery, and putrefying from access of air, forms an active poison, is in part absorbed, and brings on putrid fever." But such passing surmises attracted little attention.

The enormous mortality occurring in Lying-in Institutions, both in this country and abroad, could not fail to startle and shock those who knew the facts. When we look back on what occurred it seems almost incredible. It will probably be now generally admitted that it is safer for a lying-in woman to be delivered in a well-conducted Lying-in Hospital than in the most luxurious house, of which the hygiene and arrangements are not thoroughly within our control. Yet not very long since in these very same buildings the mortality was at times so great that every woman entering them held her life in her hand, and ran a risk not less than that of some grave surgical operation. This is no exaggerated statement; the history of obstetrics is full of accounts of these so-called epidemics of puerperal fever, now happily unknown, in which the disease spread from one case to another, or rather was conveyed from one case to another, with appalling frequency. Thus in the years 1760, 1768 and 1770, it prevailed in London to such an extent that in some of the Lying-in Institutions nearly all the patients died. Of the Edinburgh Infirmary it is said that "almost every woman, as soon as she was delivered, or perhaps about twenty-four hours after, was seized with it, and *all of them died*." In the large Maternity Hospitals of the Continent the mortality was equally great, and outbreaks of puerperal disease occurred in them all, even down to comparatively recent times, when they were checked by the general introduction of antiseptic precautions. The history of medicine records no such triumph as this.

The starting-point of our present estimate of the nature of puerperal septic disease was the well-known, but at the time little appreciated work of Semmelweiss who, in 1847, was the first to show clearly that puerperal septic disease was directly conveyed to the patient by hands, sponges and the like, defiled by decomposing animal matter; and was the first also to point out the influence of cleanliness and antisepsis in destroying puerperal contagion, by showing that students who washed their hands in solutions of chloride of lime after handling infective matter, did not convey the disease in anything like the same measure as

those who neglected such precautions. After years of calumny and neglect his epoch-making observations are now estimated at their proper value. The practical identity of surgical and puerperal septicæmia was very clearly pointed out by Sir James Simpson in his interesting paper "On the Analogy between Puerperal and Surgical Fever," which was far in advance of the teaching of the day. It is interesting to note how he foreshadowed the enormous gains both to surgery and midwifery which have followed the general adoption of the principles of antisepticism. "I do believe," he says, "that if any man should ever have the good fortune to detect, or suggest any simple and practical measures to avert and prevent, or to mitigate and cure surgical and puerperal fever, he would, in doing so, confer one of the greatest of all possible benefits upon the advancement of surgery and midwifery, and be the means of saving numerous lives in operative and obstetric practice. Nor does it seem utterly hopeless to expect the possible detection of some such measures in the way of prevention, at least, if not in the way of cure." Happily the man has been found, with the results, as regards the mortality of public Lying-in Institutions, which Simpson predicted, and all the world knows.

Unfortunately, as Dr. Boxall has clearly shown, as yet there is no corresponding improvement in the general puerperal mortality of private practice. It takes a long time for the paramount importance of the somewhat irksome details of antiseptic midwifery to be generally appreciated. To the bulk of the practitioners educated before the new doctrines were taught in the schools, such notions probably appear new-fangled and useless, and the uneducated midwives practising all over the country probably never even heard of them. In a decade or more, when the students of to-day are in active work, there is good reason for hoping that the general decrease in the mortality and morbidity of childbirth which has followed the introduction of strict cleanliness and asepsis into Lying-in Hospitals will be apparent in general practice also.

The recent development of bacteriology, and the recognition of the existence of infective germs which may be conveyed to the lying-in woman in various ways, have entirely altered the views formerly held of the nature of the puerperal fevers, whose identity with the septic diseases following surgical operations is practically conceded. The risk now seems to be, not that the influence of bacteria in producing puerperal diseases should be insufficiently recognised, but that causes of puerperal disease difficult thus to explain, but of which there is strong clinical evidence, should be discredited or disbelieved because they do not readily accord with the new views. In this there is grave danger, since it may lead us to overlook sources of disease which might otherwise be guarded against or removed.

Etiology. — It is generally conceded that puerperal septic disease is strictly analogous to surgical wound fever [*vide* art. "Septicæmia"]. It

may be well, however, to indicate very briefly the present state of our knowledge of some special questions concerning the puerperal form of the disease.

First, as regards bacteriology, it seems to be pretty clearly proved that as yet no one microbe has been identified as a specific cause of puerperal fever. In the majority of cases of puerperal septic disease, however divergent in symptoms, the infection appears to be caused by the streptococcus pyogenes, which is found in great quantities, and is probably introduced from without, on the hands of the medical attendant or nurse, or by infected sponges, instruments and the like. Other micro-organisms, such as staphylococci, gonococci, and (as has been shown in one case) the bacterium coli have, however, been detected, and may be effective either alone, or in combination with streptococci, in causing febrile processes in lying-in women; and it seems probable that other varieties of pathogenetic micro-organisms may have like effects. Diseases originating in this way correspond to those which were formerly described as "heterogenetic," the sources of infection being external. It is to be noted that these same varieties of micro-organisms are found in erysipelas, certain sore throats, and surgical wound fever. There is, indeed, an important class of puerperal diseases, originating in the decomposition of portions of organic matters in the genital tract (such as blood-clots, detached portions of placentæ, membranes, and the like), which were formerly described as "autogenetic"; it is pretty clear, however, that this term is not strictly applicable to cases of this kind, for had not these retained matters themselves become infected from without, no septic mischief would have resulted. It has been supposed that cases of this kind are "sapræmic," the mischief arising from the absorption of poisonous ptomaines resulting from their decomposition: it is, however, recently contended that sapræmia of this kind is not by any means so common as has been supposed; pure cultivations of streptococci are generally to be made in these cases, and they are probably due to infection from ordinary pus producing organisms.

Whether strictly "autogenetic" poisoning may occur in puerperal women, from pathogenetic organisms existing in the genital tract before delivery, is a question which has been hotly discussed. It is supposed that such organisms, having no effect during pregnancy, may become dangerous when absorbed through the lesions of continuity occurring during labour. A large number of observers have examined the vaginal and uterine secretions in women after delivery, and those of the vagina during pregnancy. The general result is that both before and after delivery micro-organisms, generally streptococci, are to be found in the vaginal secretions, which do not exist after delivery in the uterine discharges unless febrile symptoms be present, when they are found in abundance. This being so, auto-infection is theoretically possible. It is probable, however, that it is of rare occurrence, since Leopold and others, on abandoning the use of antiseptic douches before and during labour, found that the number of febrile cases in their practice was lessened considerably.

That strict antisepsis of hands, instruments and the like is of primary importance in midwifery practice has been clearly proved by the remarkable results which have followed its introduction into Lying-in Institutions in all parts of the world. No satisfactory explanation, however, has as yet been offered of the extreme susceptibility of puerperal women to the influence of pathogenetic micro-organisms. It is clearly not their absorption through lesions of continuity in the genital tract which is alone at fault; such lesions continually occur in women who have undergone operations about the vagina and uterus, when micro-organisms must be present as they are after delivery, and yet nothing analogous to puerperal fever occurs. There must, therefore, be something besides the mere presence of micro-organisms, something which is special to the lying-in woman, which predisposes to this type of infection; what is it which causes her structures to afford so favourable a soil for the growth and development of such micro-organisms as may have gained access to them? In the answer to this question the explanation of the proclivity of lying-in women to septic disease will no doubt be found, but as yet no very satisfactory answer can be given. The hydræmic condition of the blood existing during pregnancy, and the fact that immediately after delivery a quantity of excrementitious matter is absorbed into the circulation during the process of involution, suggest themselves as possible factors in this susceptibility; but further investigations in this direction are still much needed.

Of late years there has been a tendency on the part of obstetricians to limit the causes of puerperal infection to pathogenetic matter conveyed directly on the hands, instruments and the like, and to minimise the influence of contagion conveyed in any other way. There appears to be, however, strong clinical evidence that infective material suspended in the atmosphere may reach the patient by some other means than by direct conveyance. Dr. Amand Routh, in a discussion on this matter at the Obstetrical Society, referred to a case occurring in the wife of a butcher who was confined over the shop. I have myself been called in to no less than three such cases in butchers' wives. In some of these the odour of meat permeated the whole house. Is it not probable that infective germs, similar to those which convey the contagion in the case of students engaged in dissection, were widely diffused, and that no lying-in woman is safe in such an atmosphere?

A number of cases have been brought forward by myself to prove the origin of puerperal disease in defective sanitary surroundings. Similar cases have been published by Gueniot and many others; and it appears beyond doubt that here is a fertile source of a dangerous kind of illness in lying-in women, which has never yet been clinically distinguished from puerperal septicæmia due to manual and like conveyance. Is it to be assumed, as some seem inclined to assume, that this illness is something entirely different from septicæmia, merely because they do not admit that pathogenetic microbes can be suspended in the atmosphere as well as attached to examining fingers? It has been suggested that

as the air of sewers has been proved to be bacteriologically pure, these cases may be explained on the supposition that sewer air alone does not cause septicæmia, but produces, possibly by some unrecognised ptomaine contained in it, a condition peculiarly favourable to the growth and absorption of pathogenetic germs after delivery. This hypothesis would account for cases, otherwise difficult to explain, in which women, who have been exposed for a length of time to sewer emanations without apparent mischief, show signs of septic disease as soon as labour has taken place.

There is also good clinical evidence that a form of puerperal disease, hitherto not distinguished from septicæmia, may arise from the conveyance of the poison of such zymotic diseases as scarlet fever or erysipelas, in which the characteristic symptoms of these diseases respectively are not present. It is impossible in a paper of this description to bring forward this evidence, but it exists in abundance. It has been supposed that Dr. Boxall's excellent researches disprove this position. What Dr. Boxall has proved, and very conclusively, is that scarlet fever, and presumably erysipelas and other forms of zymotic disease, frequently breed true in lying-in women, and run a normal course. This, so far as I know, no one has ever denied. He has not, however, proved, although the inference has very generally been drawn, that such diseases always breed true. There is, indeed, strong evidence to the contrary; and it seems impolitic and illogical to shut one's eyes to recorded facts, and to say — as many do — because they do not fit in with certain opinions on the causation of puerperal septic disease, "This is a mere coincidence, and in these special cases the infection must have been conveyed from some other source." It is not very easy to explain why the poison of zymotic disease should in one lying-in woman produce a typical case of the originating disease, and in another an illness indistinguishable from septicæmia. It may be that in the latter case the channel of entry is through lesions of continuity in the genital tract. All I can now say is, that the evidence of the origin of certain forms of puerperal disease in this way is very weighty, and as yet has never been shaken.

Pathology. — The post-mortem signs in cases of puerperal septicæmia are so various as to render any complete description impossible. In the most intense form the patient may succumb before definite pathological changes, such at least as are evident to the naked eye, have had time to appear. There may then be little more to observe than a thin altered condition of the blood, and traces of commencing inflammation in the veins and lymphatics of the uterus. Microscopically signs of diffuse mischief may be found in almost all the tissues, as shown by granular infiltration and disintegration of cell elements.

In the more chronic cases extensive pathological changes are found in many organs. The genital organs themselves are largely implicated. The vagina will generally be found inflamed and œdematous, and any lacerations about the perinæum or cervix swollen, especially at their edges,

and covered with a dirty yellowish membrane. This membrane is chiefly formed of pus cells and necrosed tissues, and, in the event of recovery, is thrown off, leaving a healthy granulating surface beneath. The tissues of the uterus show signs of œdematous infiltration, and become soft and swollen. The endometrium is covered with a purulent débris; or it may become necrotic, and the underlying tissues bared or partially destroyed in portions. The lymphatics are especially enlarged, and their dilated cavities filled with a yellowish fluid consisting of pus and masses of cocci. From them inflammation spreads into the para-metritic connective tissues all round the uterus, between the folds of the broad ligaments, and even into the iliac fossæ; and this may eventually resolve or may terminate in abscess. Salpingitis and ovaritis are generally met with, and the canals of the tubes may also be filled with infected pus.

Some form of peritonitis is almost always present. This may be limited to the neighbourhood of the pelvis, and then the folds of the peritoneum are matted together with exudation. Diffuse general peritonitis is of very common occurrence, the pathogenetic matters being conveyed through the inflamed uterine lymphatics, or along the tubes to the peritoneum. Then follow very various results of the peritonitic affection. The cavity of the peritoneum is filled with an offensive serous fluid, the surfaces of the intestines are covered with a fibrinous exudation, their muscular tissues are swollen and œdematous, and they are often enormously distended with flatus.

Other serous cavities are often attacked, probably through the lymphatics which have been found full of bacteria at great distances from the uterus; and marked inflammations of the pleuræ, the pericardium, and even of the larger joints are common.

Thrombi in the veins may play an important part in the pathology of the disease, as they may become infected by bacteria conveyed to them in the blood. In the course of the changes naturally occurring in these blood-clots they soften, and minute infective emboli detached from them may be carried to distant parts of the body, and there, becoming impacted, may give rise to multiple abscesses, pneumonia, and other complications of the septic process.

Symptoms. — As puerperal and surgical septicæmia are due to like causes, so are the resulting symptoms much alike.

The first symptom to be observed is an initial rigor, which may be so slight as to escape notice; but on inquiry it will generally be found that the patient had complained of chilliness, which attracted little attention at the time. This may occur as soon as twenty-four hours after delivery, more commonly on the third or fourth day, and rarely, if ever, after a week. Puerperal illnesses commencing later are of doubtful septic origin, as in cases in which the distinct influence of sewer gas emanations are traced; or, it may be, that the initial symptoms were so slight as to escape observation, until some secondary complication, such as pelvic inflammation or phlegmasia dolens, appeared. During a

protracted septic process fresh rigors may from time to time occur, due to the absorption of more poison, as in cases in which putrefying organic materials remain undisinfected in the passages; or in the pyæmic type of disease, in which coagula formed in the veins soften and break down, and infective emboli, becoming thus detached, are carried to and arrested in distant parts of the body.

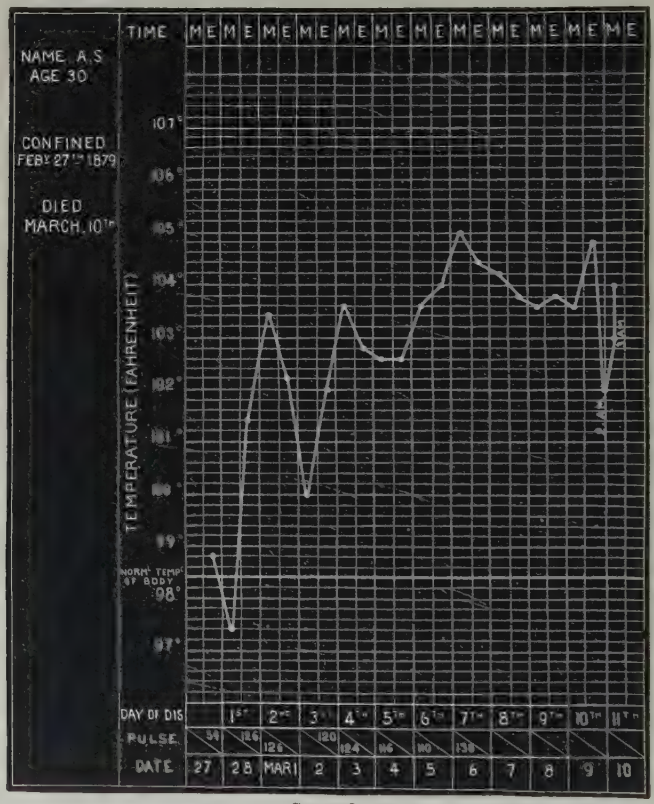

Chart 2.

Following the initial rigor, *fever*, indicated by elevated temperature, is always present, and continues until death or convalescence. There is no very definite period of the pyrexia, which varies according to the nature of the case, the intensity of the poison, the occurrence of secondary complications, and the like. In the accompanying Charts, copied from my *Treatise on Midwifery*, these variations are well shown. Sometimes (as in Charts 7 and 8), it remains uniformly high — from 102° up to 104° or 105° — even during a protracted illness, until convalescence or death; at other times (as in Charts 5 and 6), it shows marked remissions and exacerbations, the latter probably being caused by fresh absorption of septic materials. With fever the pulse is always frequent,

ranging in bad cases from 120 to 140, and becoming thin, compressible, and even imperceptible.

The other symptoms of septicæmia vary considerably with the type of disease which is present.

In the most intense cases (such as were formerly so often seen in Lying-in Hospitals, but now happily rarely met with), the patient may

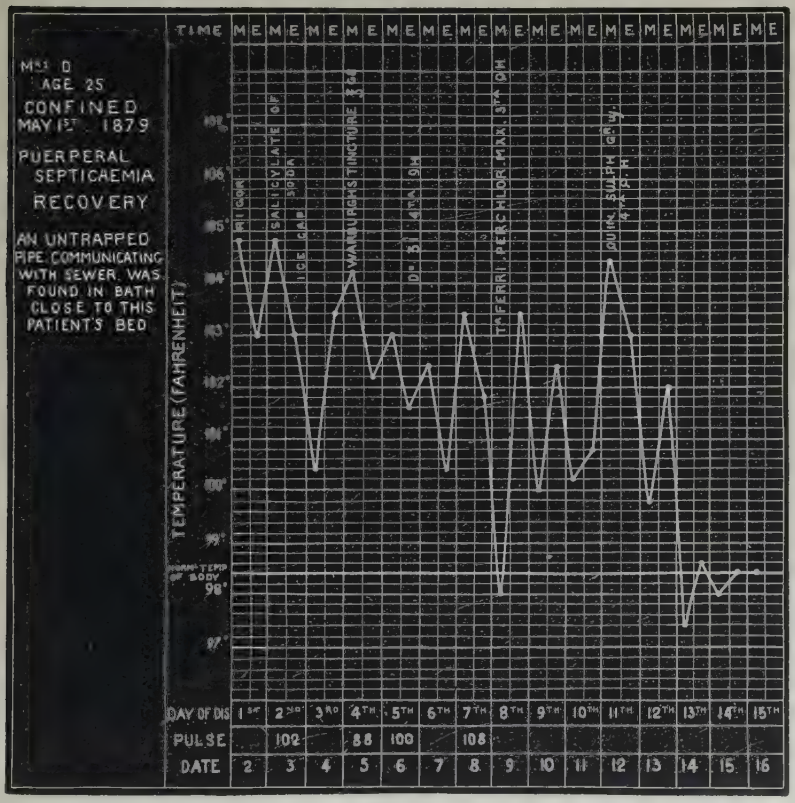

Chart 3.

be overwhelmed from the first by the intensity of the disease. The temperature ranges from 104° upwards, with little or no remission (as in Chart 8) the pulse is rapid, small, compressible, running up to 140, or it may even become uncountable. The countenance is sallow and anxious, and the tongue dry and furred; the intelligence as a rule is unimpaired, although towards the end there may be low muttering delirium.

In a type of disease which is not so intense, but analogous in character, and in which the septic poison is probably absorbed through the lymphatics, the symptoms are of the same kind, but not so severe. The

illness generally commences within three days; in Charts 2, 6, and 8 it will be seen to have begun on the second day. The fever runs high, even to 105°, and it may continue elevated for three weeks and upwards, as in Chart 7. More frequently the disease ends in one way or another within a fortnight. The pulse is rapid, thin and compressible. The tongue may be clean, or even dry and cracked, but this generally occurs when too much stimulant has been given. In such cases extreme distension of the abdomen is usually a marked symptom, not due to peritonitic effusion, but to paralysis of the intestinal muscles, and to excessive flatulent distension. It is not, as a rule, tender on pressure, and generally, even when the illness is intense, the patient makes no complaint of suffering. The bowels may be constipated; but sometimes, and as the disease makes unfavourable progress, uncontrollable diarrhœa supervenes. Vomiting of dark, grumous, coffee-coloured matter is sometimes present. The respiration is often hurried and panting, and if the pleuræ or pericardium become affected, characteristic friction sounds may be heard. The skin is at first dry and burning, and frequent mottled red septic rashes, of an erythematous character, may be seen about the chest and abdomen; later in the disease profuse perspirations are of frequent occurrence. The intelligence as a rule is not much affected: the patient may be dull and heavy, and she is generally unconscious of the peril in which she is placed; but her faculties may otherwise be clear to the end. At other times delirium, but never of a very intense type, may be present.

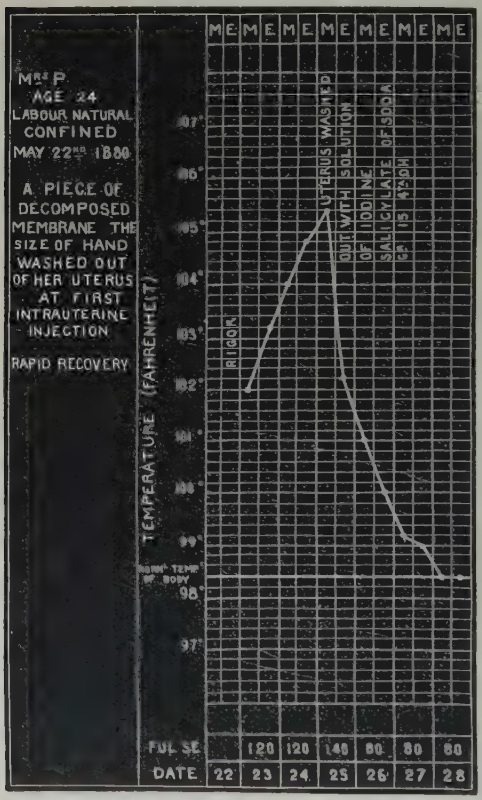

Chart 4.

The cases in which the venous system is more especially affected are, as a rule, more protracted in their course, and more marked in the remissions which may occur; the temperature falling nearly to normal, and again rising, after a fresh rigor, from the causes already described.

When the septic process leads to perimetritis or parametritis the

symptoms are modified accordingly. Much more abdominal pain is felt, and there are always characteristic local signs depending on exudation in and about the pelvis, involving the peritoneum or the connective tissues. This may be absorbed if the case run a favourable course, or the inflammation may run on to suppuration, and end in pelvic abscess.

In the more purely pyæmic cases we may have prolonged elevation of temperature of a hectic type, with morning remissions, and the

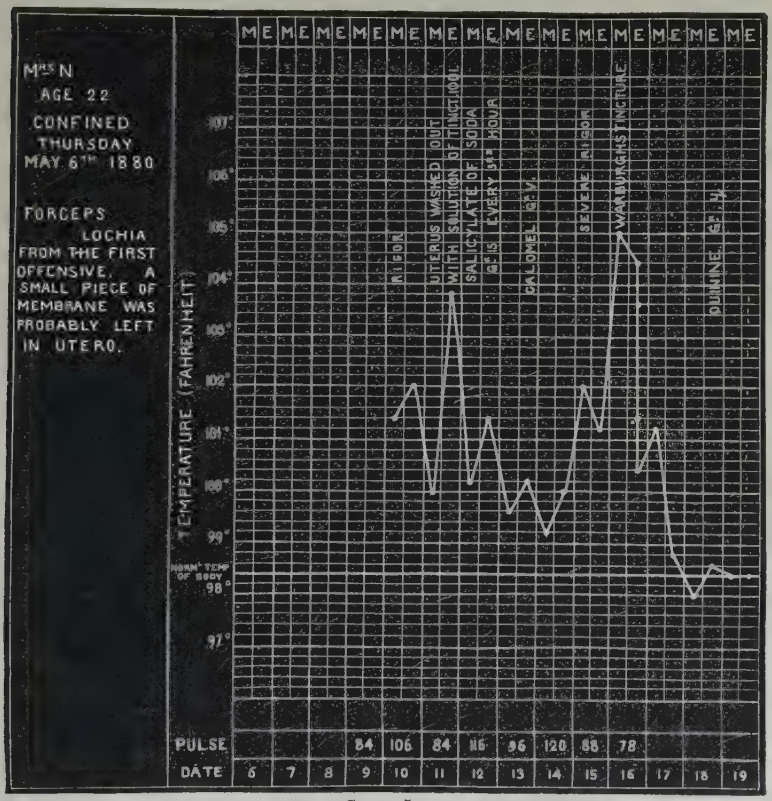
Mrs N
AGE 22
CONFINED THURSDAY MAY 6TH 1880
FORCEPS
LOCHIA FROM THE FIRST OFFENSIVE. A SMALL PIECE OF MEMBRANE WAS PROBABLY LEFT IN UTERO.
TEMPERATURE (FAHRENHEIT)
107°
106°
105°
104°
103°
102°
101°
100°
99°
NORM. TEMP OF BODY 98°
97°
M E M E M E M E M E M E M E M E M E M E M E M E M E M E
RIGOR
UTERUS WASHED OUT WITH SOLUTION OF THYMOL
SALICYLATE OF SODA GR 15 EVERY 3RD HOUR
CALOMEL GR V
SEVERE RIGOR
WARBURG'S TINCTURE
QUININE GR V
PULSE 84 106 84 116 96 120 88 78
DATE 6 7 8 9 10 11 12 13 14 15 16 17 18 19

Chart 5.

eventual formation of multiple abscesses in various parts of the body; or suppuration may occur in the larger joints. Occasionally there may be general peritonitis instead of the localised form of the disease: then the symptoms are much more intense; there is acute pain and general tenderness, and the abdomen soon becomes greatly distended from gaseous expansion of the intestines. Very constant and distressing vomiting is usually present, and such a case will generally end fatally in a few days.

It is needless to say that these symptoms may all, or some of them, be very variously mixed in particular cases. Hence the paramount

importance, when in attendance on any case of septicæmia, of carefully watching day by day for the various complications that may occur.

Treatment. — If there be one disease more than another in which the time-honoured adage, "Prevention is better than cure" should be inces-

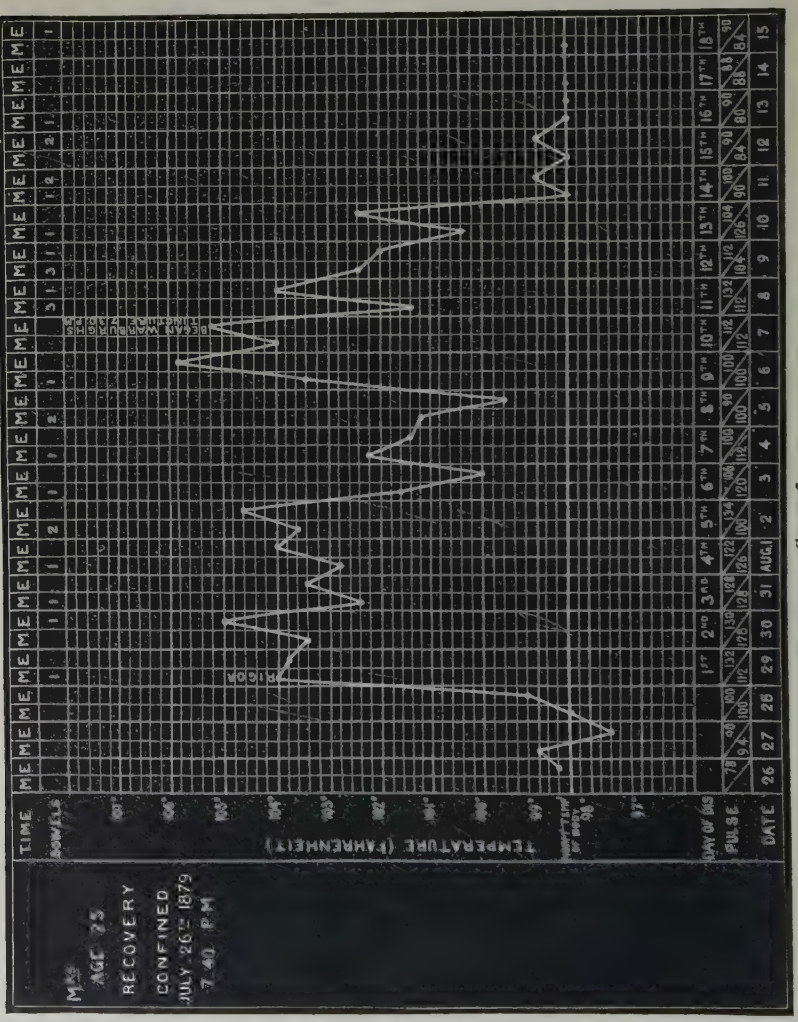

CHART 6.

santly borne in mind, it is surely puerperal septicæmia. To enter into the details of preventive treatment, however, would involve a recapitulation of the whole subject of practical attendance on lying-in women, especially of antiseptic midwifery, to the importance of which all students,

practitioners, and nurses are now, it is to be hoped, thoroughly alive. Briefly, absolute cleanliness of hands and instruments; the disuse of sponges; the thorough washing of the hands, first with soap and water, then with antiseptic lotions (such as the 1 in 1000 solution of perchloride of mercury); the judicious use of antiseptic douches before and after

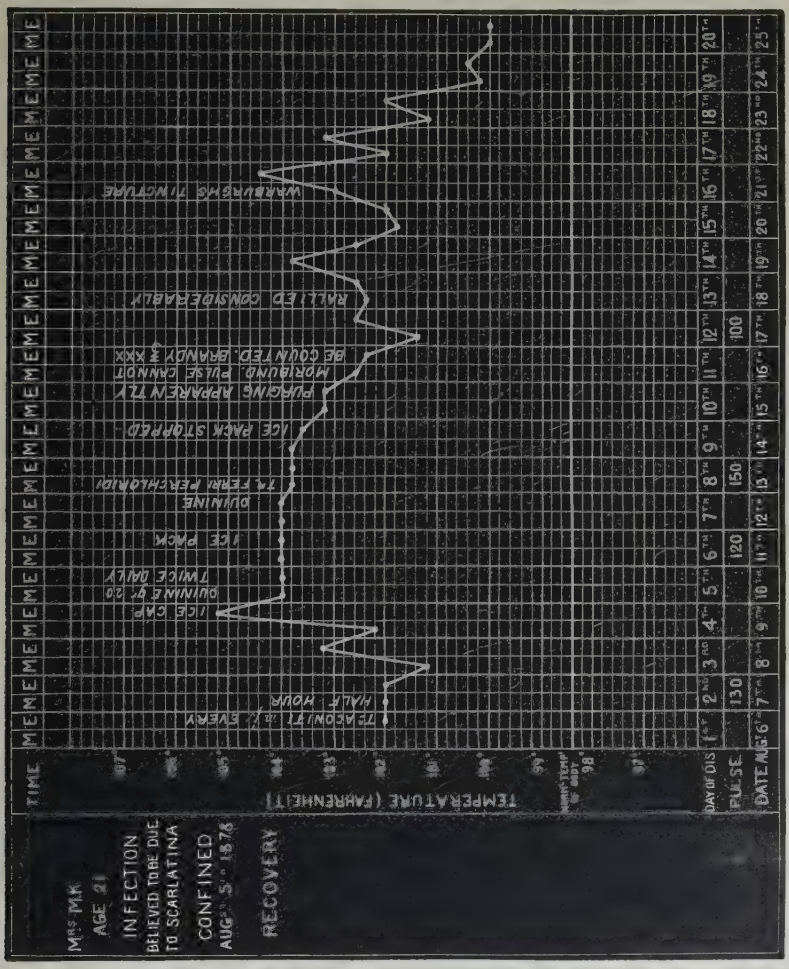

CHART 7.

delivery and during convalescence; the avoidance of needlessly-repeated vaginal examinations; the closure with aseptic ligatures of all attainable breaches of continuity in the genital tract, such as lacerations of the perinæum; attention before delivery to such questions of hygiene as drainage, the avoidance of contagion, and the like, form the main headings of this all-important topic.

When once the conflagration has begun, it may now and again be possible to extinguish it soon by removing any obvious source of mischief, such as by washing away decomposing materials in the genital tract, the removal of the patient to a fresh and unvitiated atmosphere, and so on; but more generally our aim must then be to watch the patient until the septic process has burnt itself out, to minimise its ravages, and to keep her alive until the imminent danger is over.

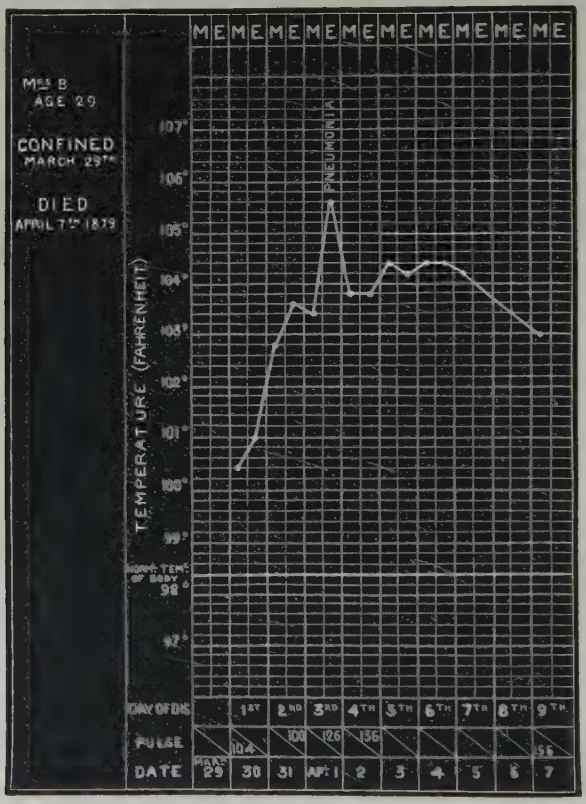

Chart 8.

On the first advent of threatening symptoms the possible presence of any removable cause of septic infection should be carefully investigated.

It will be well to make a thorough local examination to see whether there be any sloughing surfaces about the vulva, or a lacerated perinæum, which, if lacerated, should be disinfected as completely as possible by scraping, dusting with iodoform, and the like. One or two irrigations of the uterine cavity, which should be administered by the practitioner himself, may cut short a threatened attack by washing away

infecting organic matters. Tincture of iodine dropped into warm water until it is of a dark sherry colour, a solution of creoline in water, or a 1 in 2000 solution of perchloride of mercury, are amongst those which are most effective. Subsequently antiseptic vaginal douches should be given night and morning. The value of such antiseptic irrigation of the uterine cavity cannot be exaggerated in any case in which decomposing portions of membranes and the like are retained in utero. It is not uncommon under such circumstances to see very threatening symptoms at once cut short (Chart 4), and there are few cases in which they should not be administered. To be effectual, however, the irrigation must be thorough, and it is useless to trust it to the nurse, as is frequently done. Two or three intra-uterine douches should be sufficient, and as the process is often painful, and always annoying to the patient, it is rarely needful to continue it. Of late, especially in Vienna, curettement of the uterine cavity, followed by swabbing with linimentum iodi, has been much recommended. It is likely to be very useful when there are portions of retained placenta in the uterus; and in skilled hands it is a very effective way of thoroughly disinfecting the uterine cavity, but it requires a certain aptitude and experience, and the procedure is not free from risk.

The sanitary condition of the house should be investigated and, if found defective, the patient should be removed at once to another room, or even to another house, if practicable. In any case it is often useful to remove the patient from the lying-in chamber, the atmosphere of which must generally be unwholesome from long occupation, even if it be not otherwise tainted. It is impossible to exaggerate the importance of thorough ventilation, and of a plentiful supply of pure fresh air. I have frequently been struck with the improvement following this simple procedure.

The general treatment resolves itself into measures for supporting the strength of the patient during the progress of the disease, and into the administration of such drugs as are likely to alleviate the symptoms and to lessen their intensity.

The former indication is best met by administering an abundance of easily assimilated nourishment at frequent intervals, say every second or third hour, such as strong beef tea, Brand's essence, milk, eggs beaten up with milk, and the like; and nowhere is the value of trained and efficient nursing more apparent than in the conduct of this important part of the treatment. In a disease in which there is generally a marked tendency to prostration stimulants will sooner or later be required. It must be admitted that they have often been given in needless excess, an error which it is necessary to guard against; nevertheless, in bad cases their use in moderate quantities (such as a tablespoonful of good old brandy or whisky every four or six hours) will be very valuable, strictly proportioning the quantity to the degree of debility and prostration. In very severe cases, in which the pulse is rapid and thready, and there is much low delirium, tympanites and sweating, their free use in larger quantities may be necessary to save the life of the patient.

Medicinally drugs which lower the temperature are most useful. In an early stage probably antipyrine in doses of 20 grains, combined with 30 minims of sal-volatile to counteract depression, answers best; or in its place 2 or 3 grains of salicylic acid, or salicylate of soda, may be given. These cannot, however, be continued more than a day or two, and later it is best to trust to the antipyretic action of quinine. Quinine is not uncommonly given in small doses of 5 grains thrice daily, but I much prefer to administer it in full doses of 20 grains night and morning; this will often reduce the temperature two or three degrees. It may be advantageously combined with 15 or 20 minims of tincture of perchloride of iron, with a drachm of glycerine, thrice daily. The iron is unquestionably a valuable drug, and the glycerine, by its antiseptic properties, seems to lessen the distressing tympanites which is frequently present. In a protracted case it is often advisable to change the drug; and, not rarely, when other antipyretics have failed, two or three doses of Warburg's tincture have proved very efficacious in reducing the temperature (Charts 5, 6 and 7).

In cases marked by hyperpyrexia, with a temperature reaching 105° and upwards, cold may be advantageously tried to bring down the body heat. One of the best ways of applying it is a Thornton's ice-cap, by means of which a current of iced water is kept running continuously round the head. It is comforting to the patient, and often relieves the throbbing headache from which she suffers. When in use it often brings down the temperature two or three degrees. The external application of cold, by sponging or by the use of towels soaked in ice-water, may be tried in very severe cases; but this treatment is troublesome, and as it is palliative and not curative, it is not often called for.

The only other remedial means specially calling for notice is the use of aperients, formerly much employed. In the early stage of the disease one or two doses of calomel (of 4 or 5 grains each) certainly seem to act well, and may generally be administered with advantage. It is to be remembered, however, that as the disease progresses diarrhœa, often uncontrollable, is very apt to supervene, and aperients should therefore be employed with caution.

It is to be hoped that further research will give us some means of counteracting the septic state of the blood; and it is not unreasonable to look for some valuable aid in this direction from the advances now being made in sero-therapeutics.

Abdominal section has been much discussed of late years in connection with puerperal septicæmia. The successful cases have been chiefly where localised collections of pus were present, as in pelvic peritonitis, or in diffuse general peritonitis occurring six or seven weeks after the commencement of the disease. Although septic in origin, such cases can scarcely be called true cases of puerperal septicæmia. In the acute form of the disease, with great abdominal distension, laparotomy would not only be a most difficult and hazardous operation, but since the septic infection is general and not local, would promise little or no hope of benefit, even if practicable.

In every case special events and complications may present themselves for which no exact rules of management can be laid down, and which must be dealt with on general principles as they arise

W. S. PLAYFAIR.

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W. S. P.

FURUNCLE

(BOILS)

A FURUNCLE is accompanied by intense inflammation of the entire thickness of the skin, and of the underlying connective tissue. It commences with thickening and induration of the dense tissue immediately surrounding a sweat gland or hair follicle, and produces a slight elevation of the skin, which rapidly increases until the third or fourth day, when it attains its full development. The area which it now occupies depends upon the density of the skin and the facility with which infiltration has occurred. Sometimes it has a diameter of one inch, at other times of more than five inches. The central portion is a dusky red and surrounded with an intensely congested zone of a bright red colour; beyond this, again, is an area which is less congested, but often contains a considerable quantity of œdema fluid. The induration about the centre is sometimes so great that the part feels like a piece of cartilage set in the softer tissues round it. Very soon a small orifice appears at the most prominent part of the swelling, and through this orifice a small quantity of purulent fluid, and later the characteristic slough, escape, leaving behind a small cavity, with ragged, shreddy, and readily bleeding walls. The slough consists of a network of coarse connective tissue, containing in its interstices a quantity of pus cells and micro-organisms.

With the escape of pus and separation of the slough the tension and pain are greatly diminished. The healing process commences in the usual manner, and finally a permanent scar results.

Situation. — Furuncles may occur on any part of the body, but the favourite seats are those parts which are subject to dirt or friction, such as the nape of the neck, the nates, the outer surface of the thighs, the auditory meatus and nostrils. They are very rare, however, on the palm of the hand and sole of the foot, and are not common upon the abdomen or scalp. They are unusual in infants and in persons over thirty, but are most common during the period of life when severe and irregular exercise is taken. This is especially noticeable in schoolboys and young men.

Etiology. — Women are much less frequently attacked than men. Persons whose general tone is impaired by poor living, or by a severe illness, are very prone to these affections; they are extremely common in persons who suffer from diabetes, and not uncommon in albuminuria. On the other hand they occur in young people while training for certain sports, more especially in rowing men, who are apparently in good health and are carefully fed.

Whatever part constitutional states may play, it is certain that the occurrence of a furuncle is impossible without the intervention of *pus micro-organisms*. Staphylococcus pyogenes aureus or albus, or both together, are invariably present, and pure cultivations of these organisms can be readily obtained by transferring a little of the pus to any of the nutrient media which are commonly used for such purposes. When inoculated into man, either in the form of pure culture or directly from a furuncle, they give rise to similar circumscribed suppurative inflammations. This has been repeatedly demonstrated by good observers. The occurrence of furuncles in successive crops is due to reinoculation from the surface, and has nothing to do with the circulation. The impetigo or scrum-pox of Rugby football players, described by Mr. Armstrong of Wellington College and other authors, seems to be traced to chafing by jerseys infested with pyogenetic cocci. Frequent washing and stoving of flannels is, therefore, very important in all such cases [*vide* art. "Impetigo"]. If the micro-organisms were carried to the capillaries of the skin by the blood stream, we should expect to find evidence of abscesses localised in internal organs. Moreover, if the skin round the furuncle be kept perfectly clean no such crops occur.

In a simple furuncle the struggle between the micro-organisms and the tissues is confined to the abscess wall; and, though inflammation and œdema may exist for a considerable distance round it, it is not possible to obtain a culture from the œdema fluid of this area. Sometimes, however, when a furuncle is large, or is rapidly followed by the appearance of others in its vicinity, the first barrier is transgressed, and the organisms travel along the lymphatic channels, causing enlargement of the glands which drain them. At other times, when the inflammation is yet more severe, this second line of defence is also broken through, and the organisms gain access to the general circulation, thus producing septi-

cæmia which may be complicated by the formation of localised abscesses, and even terminate fatally.

Treatment. — In order to prevent the further formation of furuncles the whole of the skin should be thoroughly cleansed with soap and water, and the parts around them with sublimate lotion; the furuncles must be covered with moist, warm, antiseptic compresses frequently changed, and the underclothing boiled or stoved. The patient must be warned not to touch the affected part lest he inoculate himself elsewhere. A furuncle may often be induced to abort by injecting a few drops of carbolic acid into its centre. If pus is already formed, an artificial opening may be made by the application of several small crystals of carbolic acid in succession over the most prominent part of the swelling. The surrounding skin should be protected with vaseline and the excess of acid mopped up as the crystals liquefy. The crystals may be applied with a heated needle to which they readily adhere. This plan, though painless, is a little tedious. Incisions are extremely painful, and few people will submit to this treatment. There is, however, no other method by which such rapid relief may be given, especially when the boil is large and the tension great; and in those extremely painful forms which occur in the auditory meatus and nostrils.

After the escape of pus an attempt may be made to disinfect the cavity by thrusting into it a few more crystals of carbolic acid by means of a probe. The dressings are now to be applied and changed every four hours. The double cyanide gauze, which is both absorbent and antiseptic, is the best; poultices, however, retain their heat longer, and are far more effective in relieving pain, especially when there are a number of furuncles, many still in an early stage. Unfortunately poultices are not absorbent, and the discharge is apt to collect beneath them and reinfect the neighbouring skin. This risk of reinfection can be overcome by making the poultices antiseptic. For this purpose two drachms of pure carbolic acid should be added to half a pint of boiling water together with or immediately before the addition of the linseed meal. The poultice will contain roughly 1 in 45 of carbolic acid, and will be found to destroy pus micro-organisms; and although certain spore-bearing bacilli found in the linseed, and at times on the skin, are not destroyed by it, yet their growth is entirely arrested. Children are soon irritated or even poisoned by the use of carbolic acid on the skin; less must be used for them, and a fresh poultice should be applied every four or five hours. Before applying it the skin should be freed of all discharge and well disinfected.

It is well to bear in mind that although a furuncle is a comparatively insignificant lesion, it may at times and in unhealthy persons give rise to serious trouble. Its proper treatment should, therefore, not be neglected.

The urine should be tested, and if sugar or albumin be found the recognised treatment for these conditions should at once be adopted. If the general health is good, and the furuncles few in number, no drugs are required; good plain feeding and fresh air are all that is necessary. If,

however, the furuncles are numerous and the strength failing, large doses of iron should be given. The various drugs alleged to have special healing properties in these affections are, so far as we know at the present time, quite useless. W. S. Melsome.

CARBUNCLES

The relation between a furuncle and a carbuncle is a simple one. Their etiology and pathology are the same; clinically, however, they are somewhat different. A furuncle has one suppurating focus which results in the formation of a single orifice; a carbuncle consists of a number of furuncles grouped together upon a larger area, it gives rise to a flattened rather than a conical elevation, and results in the formation of several orifices or in the sloughing of a large portion of skin: a carbuncle is often attended with very serious consequences.

It occurs more often in advanced life, and is especially common in those who suffer from diabetes or Bright's disease. It begins as a firm, painful swelling which rapidly spreads. Its colour, at first red, soon changes to purple or varies in different parts so as to appear mottled. It is accompanied by a rise of temperature and considerable depression of spirits. Extensive infiltration, cartilaginous firmness, and pain are the prominent symptoms. It may attain enormous dimensions; sometimes it occupies an area as large as a dinner plate, and extends deeply into the subjacent tissues. The constitutional symptoms are correspondingly severe. It is indeed in these progressive forms of the disease that death from exhaustion and septicæmia are to be feared; even in those which are more limited and less rapid in their progress, thrombo-phlebitis and localised abscesses are by no means uncommon.

Treatment. — Bearing in mind the exhausting effects on the constitution and the liability to such serious consequences, it will be understood that the treatment of carbuncle must be energetic. A conical or crucial incision should be made under strict antiseptic precautions, and the infected tissues scraped with a sharp spoon. The cavity is then dried as thoroughly as possible and disinfected by carefully swabbing the whole raw surface with pledgets of cotton wool soaked in pure carbolic acid; but before deciding on this step we must carefully consider the size of the carbuncle and the age and vitality of the patient, remembering that, unless the incision be made early, severe hæmorrhage may occur. If we decide on incision it must be done at once. Every delay adds to the danger, not only by increasing the liability to hæmorrhage, but also by reducing the strength of the patient. During the last few years good results have been obtained by injecting carbolic acid at several points round the circumference of the carbuncle. This plan has been especially advocated for checking the advance of facial carbuncles, which are exceptionally dangerous owing to the close connections between the veins of the face and those at the base of the brain. For those who refuse operation we have to decide between hot and cold applications. If the

carbuncle be in an early stage, frequent poulticing is without doubt the best form of local treatment. It increases the vascularity and local reaction, which at the present day we know to be powerful factors in bringing about the termination of localised diseases. If, however, the carbuncle be large and shows signs of spreading, and especially if the general health be poor, ice compresses should be applied continuously in the hope of diminishing the activity of the disease, and thus lessening the quantity of poison which is absorbed into the system. It is just possible that by this means we may for a time give the body a rest, so to speak, from a burden which is proving too severe for it, and by allowing it to recover a little strength enable it finally to overcome the disease. Meanwhile the general surface should be kept very warm and opium given to ally pain.

Great care should be taken to support the strength by careful feeding, and large doses of some easily-digested form of iron should be prescribed. For old and weakly persons alcohol is essential, and, in the absence of special indications, such as glycosuria, they may be allowed to choose the drink they like best. The bowels should be carefully attended to, and the examination of the urine for albumin and sugar never omitted.

The occurrence of thrombo-phlebitis must be carefully watched for, and when detected the limb should be slightly elevated, surrounded with several layers of cotton wool, and kept absolutely at rest. Excision of the thrombosed vein is a very serious undertaking in old persons whose vitality is already much reduced. Ligature of the vein on the cardiac side, a less severe operation, may be performed if some such step seem desirable.

W. S. Melsome.

EPIDEMIC PNEUMONIA

Apart from its occurrence as a sequela of certain zymotic diseases, croupous pneumonia is met with not only in sporadic cases, but also in groups, and occasionally in more or less extensive epidemics, with clear evidence of infection from person to person. The proof of infectiveness is strengthened by the discovery that the tissues and sputa of pneumonic patients contain specific micro-organisms which can be cultivated, and have the power of reproducing the disease when inoculated into lower animals: moreover, Dr. Klein has found that animals so inoculated become centres of infection to others kept near them. Pneumonia of this kind is to be regarded not as an affection of the lung simply, but rather as a constitutional infection — a "pneumonic fever" — of which pulmonary and pleural lesions are only the local, and not necessarily constant manifestations. Perhaps it would be more correct to speak of pneumonic fevers in the plural, for it seems that more

than one kind of microbe can give rise to infectious pneumonia. At any rate some of the sporadic cases are of like nature, as bacteriological examination proves, notwithstanding the frequent absence of any clue to the source of infection and of extension of the malady to other persons. Similar obscurity often surrounds the etiology of enteric fever, diphtheria, and other diseases of the mobile and more or less saprophytic class. It is more than possible that such diseases may occur in forms so modified or attenuated as to be distinguishable with difficulty, if at all; or that their continuity may be maintained in lower animals, or even in external media such as soil.

Although epidemics have been recorded in this country for nearly two centuries much of our present knowledge of infectious pneumonia dates from 1888, when an outbreak of unusual extent and severity occurred at Middlesborough, and was carefully studied by Dr. Ballard. The ordinary clinical history, in attacks admittedly of the infective kind, may perhaps best be gathered from his observations, which were briefly as follows: —

The incubation was short, not exceeding five or seven days; and here it may be remarked that in other epidemics the latent period has seemed to be shorter still, sometimes not more than one or two days. The onset of the symptoms was sudden, with rigors, pain in the side or epigastrium, and rapid rise of temperature, often accompanied with vomiting and diarrhœa. The temperature sometimes reached 104° within a few hours; the highest point recorded was 105° on the morning of the third day. Delirium almost invariably set in, occasionally as early as the first day, but more commonly on the second or third. As a rule the physical signs of pleuro-pneumonia were observed, in one or both lungs, on the second day; but in many cases they were delayed and of slight intensity; generally speaking "the constitutional disturbance was out of all proportion to the evidence of local pulmonary disease." There was not much cough, but the sputa presented the characters usual in pneumonia. The tongue, in fully-developed attacks, was dry and brown, with moist white edges. Fatal cases for the most part terminated on the third, fourth, or fifth day of illness, or, at all events, within a week. Convalescence usually began by a *crisis* on the seventh to the tenth day. Three or four days after the crisis a *relapse* sometimes occurred, which often coincided with commencing pneumonia in the other lung. Among the *occasional phenomena* to which Dr. Ballard directed attention were hæmorrhages (especially epistaxis, which sometimes appeared to be critical), and painful swellings of the knees, ankles, shoulders, and other joints. By other observers, and in other localities, similar arthritic complications have been found to be due to the specific pneumococcus. In only one of the cases seen by Dr. Ballard was there any herpetic eruption about the mouth. The mortality was very high. Out of 682 attacks which came under observation, 143 (21 per cent) were fatal. In the workhouse the proportion was over 40 per cent; and it was exceptionally high also in certain portions of the town.

Two years later an epidemic on a smaller scale occurred at the village of Scotter, in Lincolnshire, and was investigated by Dr. Parsons. Here the more severe cases, which were practically limited to adults and aged persons, corresponded closely with the above description; but at the same time there was among children a wide-spread prevalence of a slight and ill-defined form of sickness, marked principally by headache, vomiting, diarrhœa, and some rise of temperature. Proof is wanting of the identity of these slight attacks with true "pneumonic fever," but the probability seems to lie in that direction.

Several other village epidemics of severe type have been recorded in recent years: one, for example, in the spring of 1893 at Yeadon, reported by Dr. Russell M'Lean, where the non-fatal cases ended by crisis between the third and eighth days, usually on the sixth. As early as 1875 Mr. Wynter Blyth called attention to the infectious character of the pneumonia then prevalent in certain North Devon villages.

Sometimes the prevalence has been limited to particular streets, or to certain industrial sections of the population. Still more localised epidemics have occurred in barracks, schools, hospitals, workhouses, prisons, and on board ship; usually in association with unwholesome conditions which may be thought likely to offer maximum facilities for the transmission of infection, and to lessen the resistance to disease. And, lastly, both in epidemic and in non-epidemic times, groups of cases are met with in single households, often without any clue to importation of infection from without, and here the type is frequently most fatal, and the indication of infection from person to person most convincing.

Etiology. — The incidence of attack, and case-mortality too, increase with advancing years, from childhood onwards. Thus at Middlesborough Dr. Ballard found the following relation to age, in cases which were fully recorded: —

Years of Age.	Attacks.			Deaths.			Estimated Attack-Rate per 1000 Population.	Case Mortality.		
	M.	F.	M. & F.	M.	F.	M. & F.		M.	F.	M. & F.
0 to 41	123	84	207	13	4	17	10·8	10·6	4·8	8·2
15 to 45	263	58	321	55	12	67	16·3	20·9	20·7	20·9
45 to 65	88	36	124	37	9	46	34·3	42·0	25·0	37·1
Over 65	18	12	30	5	8	13	53·4	27·8	66·6	43·3
All ages.	492	190	682	110	33	143	16·7	22·4	17·4	21·1

The usual experience is that attacks of pneumonia are less fatal, but much more common in men than in women, the net result being a higher death-rate among the former. In the Middlesborough epidemic, however, the case-mortality was lower among females, except at ages above sixty-five.

Debility, especially if due to habits of intemperance, must be counted among the most important of the conditions which dispose to infection and lessen the chance of recovery. Wherever the opportunity for comparison has arisen, the fatality has been found excessive among intemperate persons, and also among the poor and aged. Most observers agree with Hirsch in classing infectious pneumonia with the filth diseases, in the sense that its incidence and severity tend to be greatest where insanitary conditions exist, whether drainage defects, effluvia from foul accumulations, overcrowding, insufficient ventilation, or unhealthy surroundings of other kinds. Striking instances are on record in which localised outbreaks of so-called "pythogenic pneumonia" have followed closely upon exposure to air from foul drains. The effect of climatic conditions is not always clear, but it seems that cold, and especially sudden and frequent changes of temperature, are important disposing conditions; and the same may be said of absence of rain and low level of subsoil water, which connote dryness of air and soil. The Middlesborough epidemic, after extending during a period of comparative drought, appeared to be arrested by heavy rain. The seasonal curve is probably not very different from that of the aggregate of fatal "pneumonia" of all kinds, as recorded in the Registrar-General's reports, which is above the mean from November to April. Epidemics have occurred in the summer and autumn, but by far the greater number take place in the winter and spring. Occasionally there is some indication of endemic localisation, repeated epidemics following each other at intervals in the same community. The geographical distribution of epidemic pneumonia is not without interest in this connection. Hirsch recounts many epidemics in the several countries of Europe, from the sixteenth century onwards, nearly all of them presenting in a very marked degree the fatal typhoid or asthenic type which characterises these outbreaks in general. In some of the higher Swiss valleys it recurs almost annually, in the spring, and is known as the Alpenstich. In Italy and France and adjacent countries it has more than once attained pandemic diffusion, but although epidemics have been frequent in Europe during the nineteenth century "they have been mostly far apart and confined within narrow limits." North America has suffered severely, especially from 1812 to 1825; but here again the seasonal curve was strongly marked, and the prevalence was to a great extent limited to the winter and spring seasons. Both in America and in Africa the negro races have been found to be specially susceptible to pneumonia.

As already stated, the infection is probably not always of the same kind. At least three different microbes have been regarded, on apparently conclusive evidence, as pathogenetic in infectious pneumonia: an oval capsulated micrococcus, described by Friedländer; a capsulated diplococcus, by Fränkel and Weichselbaum; and a bacillus, found by Klein in the Middlesborough and Scotter epidemics. Each of these can be cultivated and inoculated upon lower animals. Miniature epidemics

have occurred among monkeys, guinea-pigs, and mice, when some of their number had been inoculated with Klein's bacillus. The same bacillus was found in several samples of bacon obtained in Middlesborough during the epidemic, and in all which came from infected houses; but the proof that infection was actually imparted to man in this way was necessarily incomplete. Evidence is also wanting as to the possibility of water or milk conveying infection; no recorded outbreak of pneumonia has been traced to such a source.

It may safely be assumed that the infection is given off, or tends to be given off, in the breath and sputa, and possibly in other modes also; and that it is acquired by inhalation and perhaps by swallowing. The facility of transmission from person to person is largely determined by lowered vitality on the part of the recipient, and by close and prolonged contact with the patient, especially if in a confined atmosphere. Whether, apart from this, the transmission requires an exceptional intensification of the virus, or is of frequent though unobserved occurrence in series of cases too slight and indefinite in character to be recognised as pneumonia, cannot be decided by the light of present evidence. Nor is it at all clear what is the true relation of epidemic pneumonia to other infective diseases with which it is not infrequently associated in locality and time, and even in sequence of attack in the same individual; such diseases are enteric fever, influenza, and malarial fevers [*vide* art. on "Cerebro-spinal Meningitis"]. It has been suggested that there may be an underlying identity, that the pneumonic fever may be in truth only a variety of one or other of those zymotics, but the bacteriological aspects of well-marked epidemics of pneumonia lend little support to this view. Dr. Klein has found the Middlesborough bacillus in two out of five cases examined in which croupous pneumonia followed influenza, so that the occasional sequence of the two different infections must be admitted.

The recognition of the infective character of croupous pneumonia at once suggests the application of ordinary preventive measures of isolation and disinfection. Treatment will be considered in another section.

ARTHUR WHITELEGGE.

EPIDEMIC CEREBRO-SPINAL MENINGITIS

SYNONYMS. — Cerebro-spinal fever, Malignant purpuric fever.

Cerebro-spinal meningitis, in its epidemic form, is a disease of which we in England have had very scanty experience. Yet there are many reasons why we should not neglect to consider it; its historical and geographical interest is great; its exact etiology is yet undiscovered;

and a country, hitherto immune, cannot expect always to escape outbreaks in the future.

This disease was unknown, or at least undistinguished, till the present century; within the nineteenth century there have been two wide-spread epidemics of it in Europe, and three in the United States.

Professor Hirsch, upon whose exhaustive writings I must largely draw, divides the history of epidemic cerebro-spinal meningitis into four periods (1).

The first of these periods ranges from 1805 to 1830. In Europe the outbreaks were then isolated and not very extensive; as at Geneva (1805), at Grenoble and Paris (1814), Metz (1815), in the province of Genoa (1815), at Vesoul (1822), in Westphalia, and possibly at some other places, as for instance, in Sunderland (1830). But in the United States this period was characterised by a wide-spread epidemic, including the New England states (1814 to 1816), and other more westerly states as far as Kentucky and Ohio (1808). Nor was Canada altogether exempt.

The second period is from 1837 to 1850. France was first attacked; in 1837 the disease began in two separate districts of the south of France — namely, Bayonne and the valley of the Adour on the one hand, Foix and Narbonne on the other — and thence spread through towns of S. W. and S. E. France respectively. In many instances the epidemic was limited to the garrison of a town; and an epidemic at Versailles appeared to be produced by the transference thither of soldiers from an infected spot. Other independent foci appeared in N. E. France, as at Metz (1839 to 1840), and N. W. France, as at Laval (1840), Brest, Caen, and Cherbourg, whence the disease also spread mainly, but not wholly, among garrisons. These outbreaks continued till 1842 and then abated, but from 1846 to 1850 a fresh series appeared, chiefly in garrison towns of N. E. and S. E. France, but also in Orleans and Paris. Throughout this French epidemic the central parts of France were the least affected.

Coincidently, and doubtless in connection with the French epidemic, there occurred an epidemic in Algiers (1840 to 1847).

Southern Italy and Sicily were severely attacked between 1840 and 1845, the disease spreading widely among the villages. In Denmark also and Iceland the disease was widely prevalent between 1845 and 1848.

In no other European country was there a severe and extensive pestilence, though minor outbreaks were reported from various places, as from Gibraltar in 1847 (2). In Great Britain certain cases appeared in Irish workhouses in Dublin, Bray, and Belfast (1846), and some at Liverpool.

The United States were again the theatre of a wide-spread epidemic, which manifested itself in the western and southern states, "at places as remote as possible from Transatlantic communication, and hundreds of miles distant from each other" (3). Somewhat later it appeared in Pennsylvania (1848), and at New Orleans (1850).

The third period, 1854 to 1874, exhibited quite a different distribution of the disease in Europe. The countries of South and West Europe (except for a somewhat wide epidemic in South Italy, an outbreak in Portugal and one in Ireland) were spared; Sweden, Germany, and some parts of Russia were the chief sufferers.

Beginning at Gothenburg in 1854, and reinforced from other foci in the south of Sweden in the following year, the disease spread through Sweden in a northerly direction. The outbreaks, which proved extremely fatal, appeared in winter or spring time, and gradually extended northwards till in 1858 the latitude of 63° N. was reached. After that year the pestilence gradually declined. The neighbouring countries of Norway and Denmark did not wholly escape.

In 1861 to 1862 there were outbreaks in Portugal.

Next Germany was widely ravaged. The disease appeared in North Germany, namely, in the eastern districts of Silesia (1863), Posen, Pomerania, East and West Prussia; and also in Brandenburg, Saxony, Hanover, etc. Southern Germany was severely attacked; beginning at Erlangen and Nuremburg (1864), the disease spread over the bulk of Bavaria, and appeared also in Hesse and Baden. The acme of the German epidemic was in 1864 and 1865; after 1866 the outbreaks became limited and scanty.

Austria and Hungary largely escaped. Russia suffered at various points, and notably in the Crimea (1867 to 1868).

At Dublin and in some other parts of Ireland (1866 and 1867) there was an epidemic which affected both the troops quartered there and the civil population. There were some scattered cases in England, namely, in Rochester and South London, and a small epidemic at Bardney in Lincolnshire.

The United States witnessed a third great epidemic. This began in North Carolina and in New York State (1856 to 1857), spread widely during the War of Secession (1861 to 1863), and afterwards covered nearly the whole area of the States, and did not subside till 1874.[1]

Hirsch's fourth period, namely, from 1876 to 1884, to which we may fairly add the next ten years, is one of quiescence. There have been no great epidemics, though limited outbreaks have been reported at intervals from divers countries. In Great Britian we may mention sundry minor attacks, as at Dublin (1885 to 1886), Birmingham and its neighbourhood (1876), Galston near Kilmarnock (1884), and certain villages in the eastern counties (1890).

Epidemic cerebro-spinal meningitis may be regarded in a twofold light: (1) as an acute specific fever; (2) as a disease which, like many other specific fevers, is characterised by certain definite local lesions.

Morbid Anatomy. — This consists essentially in an acute inflammation

[1] Stillé's table (1883) of the annual deaths from this cause in Pennsylvania showed that although the numbers dropped from 246 in 1873 to 82 in 1874, they still remained high, ranging from 56 to 90 per annum. Pepper's continuation of this table shows a sudden rise in 1884 to 124 deaths, then a decrease to 23 in 1891.

of the pia-arachnoid, both of the brain and cord, usually manifesting itself by a purulent effusion into the sub-arachnoid space. In some few cases, indeed, where death has taken place at a very early stage, no effusion may be perceptible to the naked eye, nothing more being evident than mere hyperæmia, or (it may be) cloudiness of the membranes. Even then, however, the microscope may show that they are infiltrated with cells. But most commonly the effusion is visible. This when quite recent may appear serous or simply cloudy, or it may be blood-stained, or again it may be transparent and gelatinous in consistence; but most commonly it is purulent, either yellowish and semi-solid like butter, or a purulent liquid. Such purulent effusion has, indeed, been found where death took place only five hours after the onset (4). The pus is in the sub-arachnoid space, and thus remains *in situ* after removal of the dura. Upon the brain it is distributed either at the base only or over the hemispheres, or in both places, and also upon the cerebellum. It may occur in streaks and patches along the line of the vessels, or in the recesses of the fissures and sulci, or in a more or less continuous sheet covering the whole brain. Of the cord it affects by preference the posterior aspect, and the dorsal and lumbar regions and cauda equina, rather than the cervical region; but the whole cord may be covered by it and the nerve roots as well. An effusion, though less frequently purulent, may take place into the ventricles of the brain, resulting from inflammation of the choroid plexus. There is therefore nothing to distinguish acute meningitis of the epidemic type from that due to any other constitutional cause, tubercle excepted.

The effusion consists, according to von Ziemssen, of pus cells, granules, fibrin, and mucin. Micrococci have been found in it — to which point we shall return later.

Dr. Burdon-Sanderson says the cells bear a general resemblance to pus cells, but are less uniform in size and character. They may form almost a continuous layer, or may be embedded in a granular amorphous interstitial substance.

In the two cases examined by Flexner and Barker they found three varieties of cells, namely, small round cells with one large nucleus (lymphocytes), large and more irregularly shaped cells with several nuclei (leucocytes), and larger cells of epithelioid type with vesicular nuclei, and some red blood-cells. There was an amorphous intercellular substance staining deeply with logwood; a little fibrin in one case and none in the other.

The subjacent nerve centres are also involved in the morbid process. This may be recognised to a certain extent from their naked-eye appearance — the surface of the brain being either congested, or, perhaps more commonly, sodden, soft and pale — but it is more definitely ascertained by microscopic sections. These show that the cell infiltration spreads, as we might expect, by contiguity into the superficial layers of the brain and cord, and further that it penetrates still more deeply along the sheaths of the vessels that dip into the nerve substance. Microscopic

abscesses and hæmorrhages may thus arise, and sometimes these are large enough to be visible to the naked eye.[1]

There is little to be said about the other organs of the body. The skin may exhibit the remains of eruptions. There may be marked post-mortem lividity, fluidity of blood, and ecchymoses of internal organs, as in other acute blood diseases. The skull-bones and dura are often highly congested. The spleen may or may not be enlarged. Bronchitis, broncho-pneumonia, and hypostatic congestion of the lungs may be present (the patients often dying from pulmonary embarrassment). Sometimes there is lobar pneumonia or acute pleurisy; sometimes endocarditis or pericarditis. But the meningitis is the only essential lesion.

Any description of the **symptoms and course** of this disease must be prefaced by the statement that they are liable to much more variation than is usual in specific fevers, both in different epidemics and in different cases of the same epidemic. Nevertheless there are certain cardinal symptoms; namely, on the constitutional side — fever of sudden onset, with depression of the vital powers, with or without rash; on the nervous side — pain in the head and neck, retraction of the head, and oftentimes delirium and coma: and out of the commonest symptoms and their most frequent association authors have endeavoured to construct a "*simple type*" of the disease.

In this type there may be prodroma, such as chills, malaise, headache, vague pains in the back and limbs; or the disease may commence suddenly with a rigor, fever, severe vomiting, vertigo, and above all with pain in the head, chiefly at the occiput. This pain is intense, and accompanied or soon followed by stiffness at the back of the neck, or actual retraction of the head. The pain is apt to spread down the spinal column and to radiate into the limbs and abdomen. Along with it there may be tenderness of the skin of the trunk. The eyes are suffused, the pupils (at this stage) are often small, the face pale, and the mind clear; an extreme restlessness is common, a lethargy is less frequent.

In mild cases the disease may stop short here and the symptoms pass off; in severe cases they become worse, the pain increases, the rigidity of the neck spreads down the spine, producing perhaps actual opisthotonus, the mind begins to wander, or downright delirium sets in, which may pass into furious mania. At such a stage, after only a few days' illness, the patient may die, apparently from the mere violence of the nervous symptoms.

But if neither death nor abatement of the disease take place the delirium is often succeeded by coma. The two conditions may alternate, or the coma may be persistent and eventually deepen into death. But should the coma also clear up, the patient, after a varying interval,

[1] Strümpell, who has drawn special attention to this process, believes that the inflammation thus set up is by no means limited to the surface of the brain. He also thinks that a large localised abscess may arise after, and in consequence of an attack of epidemic cerebro-spinal meningitis.—*Deutsches Archiv f. klin. Med.* xxx. pp. 523 foll.

and in an extreme condition of emaciation and enfeeblement, enters on a tedious convalescence.

Other common events are — (1) cutaneous eruptions, notably herpes, and petechial spots; (2) affections of the eye and ear, which too often prove irremediable.

The duration of the attack varies greatly — from two or three days to three or four weeks or more. Death may occur, or recovery set in, at variable stages, and such recovery may be complete, or may leave the patient with persistent headache, or crippled in limb or special senses.

Numerous other types are described. The most important of these is the "type foudroyante" of French authors, which may also be called the fulminant, siderant, apoplectic, or *malignant type*. The characteristics of this are extreme suddenness of onset, severe collapse, and early coma, which may prove fatal ere diagnostic symptoms have appeared. Cutaneous hæmorrhages, often extensive, are common in this form of the disease. Recovery is a rare event. Such cases are comparable to the malignant forms of measles and of other specific fevers, in which the patient, overwhelmed by the poison, dies early. They are said to be most common at the commencement of epidemics, and obviously this must render the diagnosis of their true nature more difficult.

The *abortive type* is that in which the patient suffers for a short time and in a limited degree from vertigo, headache, occipital pain and the like, but recovers rapidly without any serious illness. Similarly during cholera epidemics cases of simple diarrhœa are often prevalent; and during epidemics of scarlet fever or diphtheria cases of sore throat.

The *intermittent type* is a curious variety. In this there appear alternate remissions and exacerbations of the symptoms. Sometimes these appear to have the periodicity of true ague; but according to von Ziemssen the regular use of the thermometer shows that the periodicity is more apparent than real. This peculiar tendency may be observed in any stage of the disease, even in the prodromal period where such exists.

The clinical features of the disease must be considered more in detail; and first, the general features. Acuteness of onset and violence of local symptoms are dominant facts. Yet *the temperature* does not necessarily run high. All authors agree that the temperature is not characteristic, it neither corresponds to the type of any other fever, nor has it a type of its own. Maintained elevation of any high degree is exceptional; 101° to 103° appears to be about the average. But, as in other diseases of the nerve centres, sudden rises may take place, which are either transitory or prolonged into veritable hyperpyrexia. Neither can any rule be laid down about the *pulse rate;* it is rarely much accelerated, except it be towards the end of a fatal coma; it may vary greatly from time to time. But in character the pulse is compressible and of low pressure, not hard or bounding; in this respect corresponding to the general loss of strength, prostration, and tendency to collapse

which from the outset form a striking feature of the disease.[1] There is no constant increase in the *respiration* rate; the character of the respiration in the early stages may be simply indicative of pain, but in the graver conditions it becomes embarrassed and "suspirious," marked, that is, "by a slow, laboured inspiration followed by a quick expiration and a long pause" (5). When in deepening coma there is a steady rise in the pulse rate, respiration rate and temperature, with blueness and a clammy skin, a fatal pulmonary paralysis is indicated. The *tongue*, except in very severe cases or towards the later stages, when a so-called typhoid condition has appeared, may give no indication that the patient has a grave constitutional disease. The *bowels* are usually confined. There is neither burning heat of *skin* nor profuse sweating. The *conjunctiva* may present a diffuse pink suffusion upon which some authors lay much stress (3); the *face* is usually pale, and till stupor or delirium intervene the expression is not dazed and heavy, but indicative of pain, restlessness and irritability.

The *urine* is normal, but sometimes contains albumin, and in hæmorrhagic cases blood; glycosuria has been observed rarely (8, 9).

The *blood*, as obtained by venesection, shows, according to Stillé, the characters indicative of inflammation; while from microscopic examination Flexner and Barker conclude that there exists in the early stages of the malady a well-marked leucocytosis, associated with certain other changes, not peculiar to this disease, which may exist in any kind of local inflammation with exudation.

The *nervous symptoms* must evidently be similar to those which occur in other forms of meningitis, but their acuteness and severity are greater.

The *headache* is not a mere dull aching, but an intense and often an intolerable pain. Without definite localisation at first, it soon concentrates itself upon the occiput and back of the neck. *Pain*, too, may affect the spinal column, and may radiate thence into the limbs and round the trunk, and into the abdomen particularly; so that in some cases abdominal pain becomes quite a leading symptom. The pain is aggravated by all movements.

Cutaneous hyperalgesia is common. This probably originates, like the pain, in irritation of the sensory nerve roots. Numbness and anæsthesia may follow as the nerve irritation gives place to paralysis.

The pain is accompanied or soon followed by another symptom, so common as to be almost pathognomonic, namely, *retraction of the head*. The head is thrown backwards (in extreme cases so far that it appears to lie between the scapulæ), the patient generally lying on his side with the legs drawn up. Dr. Burdon-Sanderson thinks this pose of the head is assumed in order to mitigate the pain in the muscles of the nucha; but most authors regard it as due to a tonic muscular spasm. Sometimes the

[1] I do not find that authors lay much stress on slight irregularity of pulse, such as is common in tubercular meningitis, though Ziemssen remarks that irregularity in rhythm is not uncommon.

extensor muscles of the whole back are implicated so that there is actual opisthotonus. The limbs also may become rigid,[1] or the face may be drawn into a risus sardonicus, or in bad cases there may be trismus. All these muscular spasms are more continuous than those of tetanus, not presenting such perfect alternations of paroxysm and remission as does that disease.

Vomiting is another early symptom; it is of more common occurrence, more severe and intractable than in most other fevers. It may occur independently of food, without furring of the tongue or other sign of gastric disturbance, and is therefore to be ascribed to the irritation of the nervous system. Vomiting in the later stages of the disease, especially when associated with coma and convulsions, is indicative of distension of the ventricles by effusion, and is of bad import (7).

There may be distressing *vertigo*, particularly when the patient lifts his head from the pillow; this may be sufficiently accounted for by the derangement of the cerebral centres, but it must be remembered, too, that sometimes the auditory apparatus is specially involved.

Twitchings of the limbs are very common, general *convulsions* may occur, but (except in children) are less frequent than we might expect, considering the amount of cortical irritation. Prolonged convulsions are a bad sign, particularly when they occur late in the disease.

Paralysis of the ocular nerves, causing squint (possibly due sometimes to muscular spasm), ptosis, dilatations and inequalities of the pupils, are as common as in other forms of meningitis. *Nystagmus* is sometimes seen. Facial paralysis may also occur. Paralyses of the limbs do not appear to be common; still they may occur, and particularly in the later stages: they may be of very various type (hemiplegic, paraplegic, monoplegic), as is evident from the wide distribution of the lesion; and may be transitory or permanent, according to the degree of damage to the nerve roots and centres.

The *tendon reactions*, according to Strümpell, may vary. Thus, in thirty-two cases examined by him in Leipzig in 1879, the knee-jerks were absent in five; in three they disappeared, to reappear during convalescence, which change was probably due to varying pressure on the nerve roots; sometimes they were lively, sometimes much increased.

Optic neuritis was found by Randolph of Lonaconing, Maryland, six times in forty cases examined ophthalmoscopically.

The mental condition we have already noticed. Extreme restlessness is often a characteristic of the early days of the disease. *Delirium* very commonly supervenes, whether it be a mere wandering at night, or a kind of rambling stupor from which the patient can be aroused by sharply speaking, or an active and often violent delirium. The access of *coma* is always a grave sign, though recovery from it is by no means impossible; the more deep and persistent the coma the worse the

[1] Kernig pointed out that by putting the patient into a sitting posture (or flexing his thighs as he lies) a certain spasm is induced in the flexors of the knee, so that this joint cannot be completely straightened out (10).

prognosis. It must not be supposed that these mental states always succeed each other in regular order; delirium may occur at the outset, and the worst type of case, the "foudroyante," is marked by early coma.

There are symptoms which cannot be wholly referred to the disease of the nervous centres, and of these the most striking are the *rashes.* These are by no means constant. In some epidemics there has been no rash; in others very various rashes have been described, as for instance erythema, urticaria, rose-spots like those of typhoid, measly eruptions, vesicular and bullous eruptions. But the most common are herpetic and hæmorrhagic rashes.

Herpes of the lips and face is so frequent that it has been called characteristic of the disease.[1] Tourdes observed it in two-thirds of his cases. Von Ziemssen says that in no other disease has he observed facial herpes to spread so widely. It commonly occurs within the first five days of the illness, but sometimes later than this; and, indeed, there may be several crops of herpes coming out at various dates. It has no prognostic significance. Eruptions of herpes may come out on the limbs and trunk, and are often symmetrical; they have been referred, therefore, to the nervous lesion as a cause. According to Klemperer, herpes labialis stands on a different footing to herpes zoster. He finds micrococci in the vesicles of herpes labialis, and thinks that this eruption indicates some acute inflammatory affection. Petechiæ were so common and so abundant in the early American epidemics that the name "spotted fever" was applied to the disease — a name peculiarly unfortunate; first, because of the confusion thereby created between epidemic meningitis and exanthematic typhus; and secondly, because in many other epidemics petechiæ have not been seen at all. This rash, like herpes, may appear early, and has little relation to the gravity of the disease.

Cutaneous hæmorrhages other than mere petechiæ are a more serious matter, as they generally indicate a severe form of the disease. In the Dublin epidemic of 1866–67 such hæmorrhagic rashes were particularly common, so that the name "malignant purpuric fever" was then propounded. Dr. Samuel Gordon, describing the condition of the skin in this epidemic, notes that there may be — (1) a coldness or blueness of the extremities or whole body like that of cholera; (2) bruises and ecchymoses like those of typhus or scurvy; (3) a hæmorrhagic eruption coming out all over the body, but chiefly in the lower limbs, dark in colour, being brown, purple, or black as ink; some spots small and round, others larger and irregular, others like large spots of very black purpura, but more mottled and more irregular in colour and shape, others raised above the level of the skin. These may be gradually absorbed, or may in some cases become gangrenous. Hæmorrhages from the mucous surfaces, for example, of the nose, stomach, bowels, kidneys, may also take place.

[1] Yet Stillé says of the Massachusetts epidemic: — "Herpes labialis was noticed in a few instances . . . it is certainly much less common as a symptom of epidemic meningitis than either the roseolous or petechial spots" (3).

There are other important possibilities, which are perhaps best reckoned as **complications and sequelæ.**

Foremost amongst these are affections of the special sense organs.

The eye may be attacked, even in the early stages of the disease, by severe conjunctivitis, or by iritis or keratitis leading to corneal opacities. Still more to be dreaded is inflammation of the deeper parts, such as a purulent infiltration of the choroid, leading to detachment of the retina, or (still worse) to inflammation and disorganisation of the whole eyeball. It is possible that this deep-seated inflammation is propagated from the meninges along the sheath of the optic nerve to the structures at the back of the eyeball. Other ophthalmic complications are optic atrophy, secondary to optic neuritis; thrombosis of the retinal veins; amaurosis without obvious cause.

Disease of the *auditory apparatus* is even more frequent than that of the eye. The onset of deafness may be difficult to time in the presence of a severe constitutional disease, particularly when there is delirium or stupor. But in some cases, at any rate, it is an early symptom. Deafness may be due either to purulent otitis media, or to disease of the labyrinth (15). In the latter case it is probable that the meningeal inflammation spreads along the auditory nerve to the cochlea and semicircular canals. If these parts are destroyed total and hopeless deafness must result; and in little children this means deaf-mutism.[1] With this is sometimes associated a staggering gait.[2]

Of less importance are *anosmia* and loss of taste, which have also been described.

Chronic hydrocephalus is a very serious sequela. This has been particularly studied by von Ziemssen (7). It would appear that in cases which survive the acute stages of the disease the meningeal exudation gradually degenerates, and is absorbed; but the pia-arachnoid becomes thickened and shrunken, and the ependyma ventriculorum hypertrophies. The ventricular effusion, probably in consequence of these cicatricial changes, either remains unabsorbed or increases in amount, albeit now less purulent and more passive in character; while the cerebral substance becomes pallid and atrophied from pressure. The symptoms of such hydrocephalus show themselves during the period of convalescence, a distinct interval having elapsed since the acute stage of the meningitis; they consist of headache and pains, vomitings, coma, convulsions. Sometimes they have a paroxysmal character, and may thus last for weeks. The onset of such symptoms at this late

[1] How frequent these aural complications may be is shown by the observations of Moos, who found that out of 64 convalescents from epidemic cerebro-spinal meningitis, 38 were deaf-mutes; 20, absolutely deaf; 5, partially deaf; 1, not at all deaf; and 32 had a staggering gait. And von Ziemssen found that, in an institution for deaf-mutes, containing 42 children, every one had become deaf-mute after cerebro-spinal meningitis, while in another of 32 inmates the number due to this cause was 22.

[2] Voltolini's disease, the symptoms of which are deafness, deaf-mutism, and staggering gait coming on after a short feverish attack, perhaps accompanied with severe cerebral symptoms, which Voltolini ascribes to primary inflammation of the labyrinth, is thought by many physicians to be a meningitis spreading to the ear.

stage of the disease must give rise to serious alarm, for though recovery from hydrocephalus may take place it is very rare.

Joint disease is not unfrequent; it is mentioned both by the older writers and by several recent authors. Sometimes the joints are painful, red and swollen, as in gout or acute rheumatism; sometimes there is a simple serous effusion, sometimes they contain pus. This last fact seems to point to the general blood state as the cause of the joint disease, rather than to a perverted trophic influence of the nerve centres. The appearance of joint affections has in some instances coincided with amelioration of the meningeal symptoms. Nonpurulent arthritis has been treated successfully by salicylates.

Pulmonary congestion and collapse are frequent, as is natural in the course of an exhausting acute disease; broncho-pneumonia may occur, and sometimes acute lobar pneumonia. It will be remembered that conversely acute pneumonia may be complicated by meningitis; this occurrence, rare on the whole, is said to be more frequent after an epidemic of meningitis than at other times (16).

Other complications, apparently of a *pyæmic* nature, may be mentioned; such as ulcerative endocarditis, pericarditis, pleuritis, peritonitis, parotitis with abscess, and diffuse abscesses in the connective tissues of the limbs and trunk. Sometimes, instead of the usual constipation there is an enteritis, which causes a dysenteric *diarrhœa.*

Lastly, a rapid and great *emaciation* accompanies the disease, which may take long to amend.

As to **treatment,** it must be admitted at once that we have no specific to arrest the morbid process. In the earlier epidemics free blood-letting was employed, not with much success: but local depletion by leeches or cups, or blisters to the temples, nucha or spine, have been much used. Such remedies are suitable only for the early stages of the disease, when they are said to relieve symptoms, and possibly to modify the local inflammation of the meninges. Cold in the shape of ice-bags is recommended for the same purpose. Mercurial purgatives have been freely given, and mercury has been used so as to produce its constitutional effect. One author writes: — "The jugular vein was opened, and blood drawn in a full stream as long as the boy's strength would permit. This was followed up by relays of leeches to the temples and mastoid processes. The mercurial plan was at the same time most energetically pursued, and blisters with mercurial dressings were applied to the head and along the spine. Yet all was of no avail, my patient died in convulsions on the fourth day." All such heroic measures in the way of bleeding, purgation, emetics, mercurialisation, and the like, are contra-indicated by the tendency to depression and collapse which may exist from the very outset. Such tendency, when present, must be met by alcohol, used sparingly in ordinary cases, liberally in those which are of the malignant type. The diet must necessarily be light at first, while vomiting and other acute symptoms prevail, but it may be increased earlier than in most fevers, as there is seldom any

gastric or intestinal lesion, and severe emaciation is common. The importance of carefully feeding comatose patients, by the rectum or by the nasal tube if necessary, need hardly be insisted upon. There is an almost universal testimony in favour of one drug, namely, opium or morphia. Burdon-Sanderson says that its advantages in calming restlessness and relieving pain after the initial symptoms have subsided seem unequivocal (in doses of $\frac{1}{8}$ to $\frac{1}{4}$ grain of opium by the mouth, or better as morphia hypodermically). Von Ziemssen says, "Morphia may be regarded as one of the most indispensable remedies in the treatment of epidemic meningitis." Stillé, going further, gave one grain of opium every hour in severe cases, or one grain in moderately severe cases every two hours, under the conviction that it is not merely a palliative, but also influences favourably the whole condition of the patient, and that the opium treatment is most useful when it is begun early in the attack.

In the later stages of the disease, for such symptoms as may depend upon meningeal thickenings and deposits, iodide of potassium is the best accredited remedy, with tonics to restore the exhausted strength. But for secondary hydrocephalus, von Ziemssen says, little can be done. Local paralyses must be treated by massage and electricity. For the severe disorganisations of eye and ear nothing can be done.

Prognosis. — The course of the disease, as already mentioned, is very variable, but the outlook is always serious. In the fulminant or malignant cases, where the patient is stricken down suddenly and rapidly passes into coma, recovery is very rare. In mild cases, at the end of the first few days, after the irritative stage of headache, vomiting, and perhaps even delirium, the disease may take a favourable turn and convalescence begin. Such convalescence is sometimes rapid, but more often slow. "The disease is distinguished by the slowness of its cure and the rapidity of its fatal issue," says Tourdes. But death may occur during the stage of delirium, or still more commonly during coma, in any case comparatively early; Simon and Sanderson say, "generally from the fifth to eighth day;" Hirsch says, "commonly within the first eight days, and as a rule between the second and fourth day." Nor are the later stages free from danger, looking to the risk of hydrocephalus and to the extreme exhaustion and emaciation.

The prognosis is influenced: —

1. By the character of the epidemic; Hirsch's tables of forty-one epidemics give all grades of mortality from 20 to 75 per cent (17); and by the duration of the epidemic, for rapidly fatal cases are most frequent at the commencement of an outbreak, mild cases towards its close.

2. In the individual case by the following circumstances: —

Absence of prodroma, sudden and severe onset, early appearance of coma, depth and prolongation of coma, wideness in the distribution of the local nervous symptoms (showing brain and cord to be alike involved), trismus, complications involving other organs — especially the lungs, the

reappearance of grave cerebral symptoms (vomiting, convulsions, coma) in the stage of convalescence; all these things are unfavourable.

As to age, Hirsch says that children and people over forty run greater risk than those of middle age. Concerning a Dublin epidemic Grimshaw says that of the children admitted to Cork Street Hospital many recovered, while the recruits admitted to Steeven's Hospital mostly died.

The **diagnosis** should in general be aided by two considerations: —

1. The knowledge that an epidemic prevails.
2. The appearance of meningeal symptoms early in the illness.

There are not many epidemic diseases with which confusion is likely. Typhus may resemble it in the rash, the prostration, and the coma; and true typhus may be complicated by meningitis: but the attack of epidemic meningitis is more sudden, there is no regular upward march and maintenance of temperature, the initial headache is more severe and persistent, and the meningeal symptoms come on early. Influenza presents similarities in the sudden onset with fever, headache, and pains in the back and limbs, and in the prostration to which it gives rise. Given coincident epidemics of the two diseases, it might indeed be difficult to distinguish severe influenza from mild meningitis; but in general the shorter course, the less serious character of the nervous symptoms, and the absence of retraction of the head, and of positive signs of organic nerve disease (such as squint, etc.), would point to influenza rather than to meningitis. Should an epidemic of meningitis begin with fulminant cases, which prove fatal before nervous symptoms set in, it may be impossible to recognise their true nature at the time. The opposite difficulty may occur when an epidemic is characterised by many mild or abortive cases; in that case minor complaints, such as rheumatism of the neck, migraine, hysteria with opisthotonus, may be taken for meningitis, and particularly febrile diseases in children beginning with convulsions, vomiting, nervous irritability, and perhaps with retraction of the head.

Tubercular meningitis (in children, at any rate) has generally a more gradual onset, a less violent headache, and a more regular course than the epidemic disease.

In acute meningitis of the ordinary type diagnosis is aided by the presence of a recognised cause, for example, suppurative disease of ear or nose, disease of bone, injury, pyæmia, or other acute illness; moreover, spinal symptoms are less commonly present.

Isolated cases of cerebro-spinal meningitis occur without obvious causation, and the recognition of them before death may be very difficult. Whether such sporadic meningitis is essentially the same as the epidemic or no, we can hardly say till we have attained more certain knowledge concerning the etiology of the two varieties. The rash which is so striking a feature of many epidemics, and which seems to assimilate them to acute fevers in general, is absent in most sporadic cases, but not invariably. It is said that sporadic cases crop up particularly in places

which have suffered from the epidemic disease, as in the Franco-Prussian war (19); if this be so, it points to the identity of the two varieties.

Etiology. — Cold contributes to the outbreak, but cannot be the sole cause. Most epidemics have begun in winter or spring, and further the attack seems in individual cases sometimes to be determined by exposure to cold. But, on the other hand, in many of the severest winters there have been no epidemics, and recrudescences of epidemics have begun during spells of mild weather. Neither is the disease known in Arctic climates, but only in the temperate and sub-tropical zones. Hirsch gives its limits in W. hemisphere from 45° N. (Montreal) to 30° N. (Mobile); in E. hemisphere from 63° N. (Sweden and Russia) to 30° N. (Jerusalem, Persia, Algiers).

It is independent of malaria, and of local peculiarities of soil and situation: this is shown by its very wide distribution over manifold countries, altitudes and soils.

It has no special predilections for race or sex; as to age, it selects principally children and adults in the prime of life. As to conditions of life, it may be that privation, overcrowding, bad sanitation,—in short, the circumstances of the very poor,—favour its outbreak, but they have never been shown to form an essential cause thereof. It has been seen alike in town and country. One fact, however, is most prominent, namely, that soldiers are especially obnoxious to it, and particularly, as it would appear, during garrison life. Recruits, too, suffer more than seasoned troops. Particular battalions or regiments, or again particular barracks, have sometimes been picked out by the disease. The counterpart to this has been seen in civil life, when a particular workhouse or school has been selected by it.

The manner of its appearance and spread is peculiar. It spreads from no one centre of origin or of activity either by contiguity or on special lines, whether lines of traffic or other mode of distribution;[1] but it breaks out at diverse and apparently disconnected foci, in separate towns, villages or tenements; and it spreads in a similar discontinuous way. In point of time, an epidemic of meningitis does not steadily mount to a maximum and then decline, but proceeds by fits and starts, crops of fresh cases appearing at irregular intervals.

Its ordinary methods of propagation are not known. It has not been traced to food[2] or water-supply. Direct propagation from one patient to another is certainly not the rule, albeit there are a few instances of this. There may be a certain infection of locality, as already said, it may hang about places where it has once appeared; and it has been transferred from place to place by human beings.

I find no statements bearing on the question of immunity, as to whether one attack protects against another.

[1] There are a few exceptions to these statements, for example, the transference of the disease when troops have been moved from place to place, and the Swedish epidemic which spread steadily in one direction (*vide supra*).

[2] The surmise of Sir Benjamin Richardson, that it is due to diseased grain has not been generally adopted.

Although epidemics of meningitis have coincided with or followed epidemics of other specific fevers, such as typhus, cholera and others, it has no constant relation with any one of them, and its history and clinical features are sufficient to stamp it as specifically different from them and probably dependent on a virus of its own.

Can we go further, and say what this virus is?

We naturally look to *bacteriology* for an answer. But bacteriologists are at this disadvantage, that since their science has established itself, there have been no large epidemics of meningitis, and therefore their researches have been limited to certain minor outbreaks. Taking these, however, as a basis, a somewhat surprising conclusion is indicated, namely, that the organism associated with epidemic meningitis is identical with or closely related to that which is responsible for croupous pneumonia.

Now, inasmuch as these two diseases appear clinically to be utterly dissimilar, it may be well to state some of the facts which seem to support the alleged connection. The micro-organism of croupous pneumonia was originally supposed to be a bacillus, discovered by Friedländer and named after him. But this bacterium has been dethroned in favour of a micrococcus[1] which bears, it is true, just sufficient resemblance to Friedländer's bacillus to allow us to suppose that the two were originally confounded. This micrococcus, which we may briefly term the pneumococcus, usually occurs in pairs (diplococcus), surrounded by a transparent, easily-disintegrated capsule. The individual cocci of each pair, when seen in the blood or in pneumonic exudate, are oval or lance-shaped (like a grain of wheat or of barley); but in most cultivation media they are round. They stain with aniline colours, but are not (like Friedländer's bacilli) decolorised by Gram's iodine solution. They grow in most cultivation media provided these are not acid. They are sensitive to temperature, so that they do not grow at the ordinary temperature of a cool room, nor at higher temperatures than 42° C. In cultivations they rapidly lose vitality, and changes may be wrought—(1) in their form, so that the cocci become more rounded and are associated not so much in pairs (diplococci) as in chains (streptococci); (2) in their virulence, so that they lose their power of generating disease till they have been passed *de novo* through the living tissue of some susceptible animal. Rabbits and mice are extremely susceptible to inoculation with the pneumococcus, so that a subcutaneous injection thereof produces at the point of injection an acute œdema or cellulitis followed by rapidly fatal septicæmia. Dogs and sheep have more resisting power, so that a subcutaneous injection produces little effect on them. But injection into the pulmonary tissue of dogs, sheep or rabbits, which have been rendered impervious to the septicæmic effect, produces a characteristic croupous pneumonia. This last fact, and the fact that the micrococcus is found in pneumonic sputum, in pneumonic exudate

[1] Described by Fränkel in Germany, Talamon and Pasteur in France, Sternberg in America; and often called Fränkel's diplococcus, or the micrococcus lanceolatus. The description in the text is mainly taken from Sternberg's *Manual of Bacteriology*.

drawn by a syringe from the chest during life, and in hepatised lungs post-mortem, are held to justify its claims to be the cause of pneumonia. A most remarkable fact is that this micrococcus is often present in normal human saliva, and inoculation of rabbits with such saliva has produced a characteristic septicæmia [*vide* article on "Epidemic Pneumonia"].

Now it would seem that when a pneumonia affects tissues other than the lung proper, this micro-organism may be found in such diseased parts; not only in the lymph upon the pleura and pericardium, which are so commonly inflamed in acute pneumonia, but in rarer complications also, such as ulcerative endocarditis; and even in disease of organs beyond the chest, as in peritonitis and (what concerns us mostly) meningitis (20, 21).

Again, diseases such as these may occur without demonstrable pneumonia. Most physicians have seen cases of acute pleurisy, the clinical course of which has been indistinguishable from that of a pneumonia, but in which post-mortem the lung is not found hepatised. In these it is not surprising to learn that the pneumococcus has been found in the pleural lymph by Dr. Washbourn (67). But it has been found also in ulcerative endocarditis (without pneumonia), idiopathic peritonitis, otitis, encephalitis, meningitis after injury, and, lastly, in acute purulent meningitis which has no obvious cause (21, 22, 23, 24).

Not that in all cases of purulent meningitis this identical organism is present. For in some there has been found a micrococcus bearing a general resemblance to it, but presenting some slight points of difference (25, 26); in others the ordinary streptococcus pyogenes; in others, again, where the meningitis occurred in connection with some acute infectious disease, such as typhoid, the organism proper to that disease (27, 28).

Yet the fact that in most cases of idiopathic meningitis which have been investigated the pneumococcus has been found, and that its introduction into the cranial cavity of animals produces meningitis, as its introduction into the chest produces pneumonia, seems to show that it may be at least a frequent cause of that disease.

From sporadic to epidemic meningitis is no great step; the bacteriological observations on this latter are as follows:—

(*a*) Jaffé, studying an epidemic in Hamburg (1879), could find no micro-organisms in the meningeal lymph.

(*b*) Giuffre, in a Sicilian epidemic of 1882, found oval cocci in the meningeal lymph, not in the blood nor in the spleen. Attempts at cultivation and inoculation failed (30).

(*c*) Ughetti, in Sicily, 1883, found micrococci in the meningeal exudation and the blood; inoculations failed (31).

(*d*) Marchiafava and Celli found diplococci, both free and within the cells in the meningeal exudation; cultures were negative (32).

(*e*) Netter states that, in an outbreak at Blois and Orleans in 1886, the micrococcus lanceolatus was found in the spinal and cerebral exudation by Widal.

(*f*) Friis, at Copenhagen, 1886, isolated and cultivated a bacterium

in the shape of short thick rods, not unlike an oval coccus; inoculations failed.

(*g*) Four cases from an epidemic at Turin, 1888, were investigated by Foa and Bordone-Uffreduzzi; they found a micrococcus which they identified with Fränkel's, cultivated it and experimented with it; injections into the cranial cavity produced acute general sepsis with cerebral and spinal meningitis. Two of their four cases had pneumonia.

(*h*) At an epidemic near Padua in 1890, Bonomé obtained from the meningeal exudation a micrococcus resembling in some degree the pneumococcus, but differing from it in the peculiar tangled growth which it forms on agar, in its inability to grow in blood serum, and in some of its effects on animals. This he believes to be the specific micrococcus of epidemic cerebro-spinal meningitis. There was no pneumonia in his cases.

(*i*) Mirto in 1891 (37), as quoted by Flexner and Barker, discovered in some epidemic cases the typical micrococcus lanceolatus.

(*j*) Herwerden (1893) (38) gives the case of a woman who died of this disease in an advanced stage of pregnancy. Cæsarean section was performed, the child lived five and a half days, and then died of meningitis complicated with pleurisy. In the meningeal exudations both of mother and child, and in the blood, the liver and the kidneys of the child, pneumococci were found. The virulence of these appeared at first to be slight, but it was increased by submitting them to the action of hydrogen and oxygen, so that injection of them into rabbits produced meningitis.

(*k*) Leichtenstern (39), writing in 1893 of epidemics in Cologne and the neighbourhood in 1885–1892, says that he found the pneumococcus in cases where there was pneumonia, but not in other cases. The special micro-organism he considers to be not the pneumococcus itself, but a variety or "specific derivative" of it.

(*l*) Lastly, Flexner and Barker, in an epidemic at Lonaconing, Maryland (1893), found lanceolate diplococci in the meningeal exudation, both free and enclosed in their cells; but their cultures and inoculation experiments did not succeed well.

Such are the *primâ facie* grounds for supposing that the pneumococcus, or some allied organism, is the cause of epidemic cerebro-spinal meningitis; but there are certainly difficulties in the way of a final conclusion.

For (1) some of the observations, especially the earlier ones, are admittedly imperfect; and some are not quite harmonious in detail with respect to the characters of the micro-organism described. We hardly know what importance to attach to small variations of this kind.

(2) It has been suggested that sometimes the pneumococcus, sometimes bacteria of other diseases, may produce epidemics of meningitis. But to admit this is to give up the notion that the disease is specific at all.

(3) As to the pneumococcus theory there are general reasons both for and against it. The wide-spread dissemination of that organism,

which seems to exist even in normal human saliva, certainly harmonises with the wide dissemination of the disease, and with the sudden appearance of it at isolated foci, without recognisable sources of infection. The variability, under different conditions, of the virulence, and perhaps of the morphology of the micrococcus, which seems to be recognised in the laboratory, may explain the paroxysmal appearance of the disease, and why it is not always with us. But this only puts the inquiry a step farther back. The question then would be, What are the external influences which, either by augmenting the virulence of the micrococcus or by reducing our resisting power, render us obnoxious to its attack? And of these we are profoundly ignorant.

And, it may be objected, if identical or closely-related organisms produce the two diseases, pneumonia and meningitis, why do they not more commonly co-exist?

Doubtless such co-existence has been observed, but chiefly, I believe, in the later and more limited outbreaks; it does not seem to have struck the observers of the older and more extensive epidemics, who would have been disposed to identify the virus of this disease with that of typhus or cholera.

We cannot then consider the question of etiology as yet settled.

APPENDIX

It may be of interest to English readers if I refer briefly to the outbreaks of this disease which have taken place in the United Kingdom. Many of these (though the Irish epidemic of 1866 and 1867 constitutes a notable exception) can scarcely be called epidemics, and some indeed are merely groups of two or more cases occurring at the same time and place. Yet their essential identity with the epidemic meningitis of the Continent and America is, in some instances, hardly to be doubted, and in others is very probable.

1807. — In 1807, at Blackaton, a small village on Dartmoor, a peculiar group of cases was observed by Gervis, the nature of which, in the absence of a post-mortem, remains somewhat uncertain, but they may possibly have been instances of this disease. There were five cases, four of them in one family, and four of the five died very rapidly. Headache, vomiting, collapse, slight convulsive movements, sore throat, and an hæmorrhagic rash are mentioned as symptoms, but no retraction of the head.

1830. — In the autumn of 1830, at Sunderland, several cases occurred, in one of which meningitis was found post-mortem (41).

1846. — The first Irish outbreak occurred in the first half of 1846; there were cases in the workhouses of Belfast, Bray, and Dublin, mostly in boys under twelve years old; and two fatal cases in the Hardwick Hospital, Dublin (42).

During the same year Whittle records cases in Liverpool, some of which he distinctly ranks with epidemic meningitis as seen in Ireland and on the Continent. Of nine such cases three were fatal. Some, on the other hand, were of a milder type.

In 1846, also, a case was seen at Haslar Hospital (44).

1846–1850. — It would seem from the statements of M'Dowell that from

the time of the first Dublin outbreak mild cases presenting symptoms of meningitis continued to appear in Dublin till 1850 at least.

Three cases of somewhat doubtful nature are mentioned at Rochester in 1850 (44).

1864–1868. — At Rochester, also, in 1864 and 1865, some four or five cases occurred, one of which was examined post-mortem (46).

During 1865 it appears that there were further cases in Dublin (47); while the succeeding years (1866 and 1867) saw the second Irish epidemic, the most severe manifestation of the disease which has yet appeared in these islands (48).

This epidemic raged principally in Dublin, but also affected other parts of Ireland, attacking both military and civil population. It was marked by great fatality, and by the prevalence of hæmorrhagic rashes, so that the name of "Black Death" was at one time proposed for it, and also that of "Malignant Purpuric Fever."

In England about the same time there were some isolated cases: two in London which were rapidly fatal (49), and one at Devizes (50) (May and June 1867).

At Bardney, a Lincolnshire village, there was a small epidemic — over nineteen cases, with one death (51).

Somewhat later, namely, March 1868, we read of four cases within three weeks at Shorncliffe Camp (52).

In 1867, too, there was a fatal case with petechial rash at Stafford, where there formerly had been two similar cases, namely, in 1865 and 1859 respectively (53).

1876–1878. — The Irish epidemic of 1866 and 1867, with the minor outbreaks which we have just mentioned in England, evidently corresponds to the great wave which had just passed over the Continent.

The next notice of the disease is in 1876, in the Midlands. Two cases occurred among the militia at Oxford (54), and an epidemic in and round Birmingham; fourteen cases were admitted to the Queen's Hospital in nine months, and there were others in the neighbourhood (55).

In the winter of 1877–1878 a good many cases were seen at Dundee, several of which had a roseolar rash, or an hæmorrhagic rash like typhus. There seems to have been evidence that the disease was contagious. One case died with rupture of the spleen (56).

At Dublin, in the commencement of 1878, there were three fatal cases within two months (57).

1884–1886. — In the spring of 1884 two cases occurred at the Seaman's Hospital, Greenwich (58), and two at the London Hospital (59); but as three of these patients were sailors the local character of the outbreak cannot be insisted upon.

In Dublin, again, during 1885 and 1886 a somewhat serious outbreak took place, largely in the suburban districts, and amongst comparatively well-to-do people (60). There were fifty-two deaths during 1885. Rapidly fatal cases with purpuric spots were not wanting (61).

In 1884 a small but very fatal outbreak took place at Galston near Kilmarnock. Out of seven cases five were fatal, some with extreme rapidity. Personal intercourse was traced between the various patients, so that contagion seemed probable (62).

At Aberdeen, in 1885, Ogston examined the body of a child which died of

acute cerebral meningitis; this he referred to disease of the nasal bones, but he notes that another child of the family died of meningitis, and that the father had symptoms of the same disease.

Similarly, near Faversham in 1886 two deaths occurred in one family from meningitis (64).

1890.—In July, August, and September 1890 (65), there was an outbreak in five neighbouring villages on the border of Norfolk and Suffolk (Oakley, Broome, Scole, Kenton, Bressingham); the symptoms appear to have been typical; there were twenty cases and two deaths: one post-mortem was made, in which evidence of meningitis was found. No cause could be assigned for the disease. In a village thirty miles away, Great Horkesly, near Colchester, there was another case. Near Malden, in Essex, some obscure and rapidly fatal cases of fever had been seen that same autumn. In certain Lincolnshire villages scattered cases possibly of a similar nature occurred; thus at Willingham, near Gainsborough, a gipsy boy died apparently from pneumonia and meningitis; at Holbeach, near Spalding, a woman died with symptoms of meningitis; and a severe though non-fatal case occurred at Gedney Hill, about ten miles from Holbeach. Two cases are said to have occurred in the preceding year near Oundle, in a village distant about twenty miles from Gedney Hill.

In March, April, May and June 1890 four cases of idiopathic cerebro-spinal meningitis were examined post-mortem at St. Bartholomew's Hospital (66).

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INFLUENZA

In attempting the description of a disease we are often in doubt how best to set about the task. Influenza offers no exception to this rule, but happily, so to speak, it has overreached itself, and by the very width of its range of action over the human body has simplified matters in a way that may not at first be apparent. Clearly the only possible presentation of a disease so multiform in its character as influenza, is to describe it first of all, in as full a manner as space permits, on its clinical aspect, and thereafter to discuss its pathology and treatment.

It is not well to pay too much attention to the disease as it has appeared in other countries. After all it is the disease as it appears here in England which concerns us; and it is too often forgotten that, although the whole world is kin, yet there are racial and climatic influences that must make some difference in the picture of disease as it has occurred here or there,—a difference which may well come in to throw light upon some of the obscure points in the natural history of a malady, but which is of less importance from the practical standpoint of its management as we have to deal with it amongst ourselves. As a matter of fact, however, the disease has departed little if at all from certain broad characters, whatever the affected area.

Description.—To present the disease at all adequately it is necessary to describe groups of cases. In actual experience all groups must

necessarily blend somewhat, nevertheless each is sufficiently distinct to demand separate mention.

All cases present, more or less, certain features in common; it will be convenient, therefore, to describe first of all what we may call common influenza. A healthy person is suddenly, one may say without exaggeration that many are instantaneously attacked with violent aching of the head and eyeballs; with a pain in the back, perhaps so severe as to resemble the onset of variola; with racking in the bones that could not be worse if they were being broken; with a general distressful soreness; sharp fever without any corresponding acceleration of the pulse, and a hard dry cough, sometimes with coryza as from a bad cold. Often enough there is some little delirium during the first day or two, and not a few cases have even been ushered in by an acute maniacal delirium. The tongue is thickly coated with a white creamy fur, it is flabby, indented by the teeth, and tremulous. The breath has often a peculiarly offensive odour, and the patient suffers from a sudden prostration, both mental and physical, altogether out of proportion to the duration or apparent severity of his illness. The spleen has been found enlarged in some cases.

The fever lasts, perhaps, three, four or five days and then subsides, leaving the patient weak and much depressed, and with a feeling of having undergone a serious illness in a short space of time. To add to the discomfort, after a day or two chills are apt to recur, usually down the back. These are followed by profuse sweats, which may be repeated again and again, and perhaps only slowly disappear some time after the more essential symptoms have entirely passed away.

The first case of influenza that I recognised occurred on December 24, 1889. The disease had not then declared itself in epidemic form in England. But, as other observers have stated, cases had occurred at any rate in the two or three weeks previously. A strong healthy man went to Manchester to play a football match. He went with a bad cold upon him, and there he became so much worse that he returned home again, by which time he was so exceedingly ill that his brother, a medical man, became much alarmed. He was delirious, prostrate, restless, with a temperature of 102°, a very distressing dry cough, a generally tremulous condition of the muscles, and a thickly furred tongue. His lungs gave no evidence of pneumonia, but the air entered badly, and there were plenty of sibilant rhonchi and rales, a state of things that indicated that the bases were engorged — "congested," as I should prefer to say. These various symptoms, combined with a little diarrhœa, gave the case the appearance of typhoid fever, but the temperature, falling almost at once to normal, led to a correct diagnosis, and he rapidly convalesced.

Of the simple catarrhal form, with its prostration and pulmonary congestion, this is an ordinary case of moderate severity; but there are cases in which the poison is apparently much more virulent, and where in consequence the disease assumes still more of the characters of typhoid

fever. A striking example of this occurred also early in the epidemic of 1889. A young healthy man came to town to spend Christmas with his relatives who were in an hotel. Within a short time from his arrival he was seized with an overwhelming drowsiness and fever. His drowsiness was indeed so great that he could by no means be kept awake, and in this respect the case corresponded to a mild attack of the sleeping form of influenza as it has occurred in this epidemic, and has been recorded as "nona" by Braun and others (1). He was removed to a nursing home because of some slight roseola which suggested scarlatina, but within a few hours he was so prostrate, with so much subsultus, and a tongue so dry, brown, and cracked, that he presented the appearance of some severe form of continued fever. There was somewhat of the dusky appearance of a case of typhus, the engorgement of lung either of that or of enteric fever, the pulse about the ordinary rate of typhoid; but the pyrexia did not run the course of either of these, and in five or six days the fever had spent itself and the man was convalescent.

Another group may well be styled "pulmonary influenza," for the violence of the disease expends itself chiefly upon the respiratory tract. There is the same sudden attack, with the aching head and limbs, the fever, the thickly-coated tongue. But the cough is more troublesome, there is more obvious impediment to the respiration, and the posterior parts of the lungs are full of sharp, sticky rales of a quality quite peculiar to the disease. This condition will often slowly increase, and extend over the lung, the fever continuing, and the condition of the patient becoming more and more embarrassed. Delirium supervenes, the pulse at last mounts up, and the case terminates fatally, without, so far as the physical signs go, any evidence of consolidation being at any time present. Sometimes in the course of the bronchial catarrh patches of solid lung will appear here and there, or an acute pleuro-pneumonia will suddenly light up. In some of these the influenza bacillus has been found, thus showing the disease in truth to be influenzal pneumonia; in others, again, only the pneumococcus, giving support to another contention that the consolidation is in some cases a sequel or complication, and not the primary disease.

When pleurisy occurs it often runs on into an empyema. In most cases, happily, the catarrh, though slow in taking its departure, gradually becomes of a less glutinous quality, and the expectoration more and more free, until the amount of the purulent discharge expectorated becomes so excessive that one wonders where it can all come from, seeing that there are seldom any physical signs adequate to so profuse a flux. Sometimes the pulmonary affection leads to hæmoptysis, occasionally profuse, and to hoarseness, and may thus have much superficial likeness to tuberculosis. Into this — the pulmonary form — the simple or common influenza often passes. There is often, indeed, a much quickened respiration, even when there are no physical signs of any pulmonary disease, and Graves (quoted by Thompson (10)) describes a dyspnœa which is not to be explained by any stethoscopic signs.

Over and over again, too, there is the history of three or four days of fever, then a return to a normal temperature and apparent convalescence; and then, after perhaps twenty-four or more hours, a relapse, not infrequently ascribed to some indiscretion in uncovering or what not, but which, in most cases, is probably a part of the disease. And with the relapse come more pulmonary symptoms — more cough, more expectoration, more fever, a gradual and too often uncontrollable invasion of the lung by the glutinous bronchitis already described, and in too many cases death eventually by the delirium and the exhaustion of a gradually asphyxiating bronchitis, or of a pneumonia that knows no crisis.

Even when the disease clears up it is very slow in its progress; the expectoration remains profuse and purulent; the lung is slow in expanding to its full extent again, and, until it has completely recovered, is very prone to temporary recurrences of the old physical signs.

Influenza that spends itself primarily and chiefly upon the heart is not a common occurrence, but it is a very grave matter when it does happen. The symptoms are a frequent and alarming tendency to syncope, and a feeble, irregular, and often a very rapid pulse.

A waiter, æt. thirty-five, who had drunk freely, was suddenly taken ill with influenza. He kept at his work as long as he found himself able — a matter of a day or two only — and then sent for his doctor. His state was as follows: He was a well-nourished man, sitting half upright in bed, with a short, panting respiration and slight lividity of the lips. His pulse at the wrist was hardly perceptible, though regular, 120 in the minute. His general condition reminded me most of cases of severe pericardial effusion, but there was no evidence of any increase of the precordial dulness, nor were the sounds muffled in any way. The impulse was diffused and palpable beyond the nipple, the first sound was metallic and flapping in character, but there was no murmur. The other viscera were in good order. The only conclusion that seemed possible was that an acute dilatation of the heart had taken place, and the man was so ill that he appeared likely to die. As a rather forlorn hope strychnia was injected subcutaneously with much apparent benefit, and he recovered.

The signs of cardiac failure are for the most part a ready tendency to fainting, a feeble, irregular pulse, sometimes pallor, precordial distress or pain, and sweating. There are records of a fatal issue under such circumstances, sometimes sudden, like the paralysis of diphtheria; at other times deferred for a few days, after the manner of acute dilatation of the heart. For example, a middle-aged man of very nervous temperament was taken ill with influenza. He was kept in bed and had no alarming symptoms, but as he flagged and was depressed he was told to get up. In the exertion attendant upon the effort he was seized with most alarming faintness, from which it was difficult to rally him — indeed, he never did rally thoroughly, for his hands and feet remained cold, his face was a dusky gray, his pulse beat 140 per minute, and was very feeble, the first sound of the heart was so feeble as to be hardly audible, he was constantly sick, and he died in about thirty-six hours.

When recovery takes place from attacks of this kind the heart may yet be long in returning to a natural action, the pulse remaining feeble, intermittent, irregular, or easily disturbed; and Dr. Sansom has recorded cases of persistent tachycardia. The pulse is sometimes unnaturally slow as well as intermittent or irregular — 40 to 50 per minute only — in this also showing a striking likeness to one of the ominous symptoms in diphtheria.

As an affection of the circulation thrombosis of one or other of the larger veins of the extremities may here be mentioned. I have seen seven cases of this complication which occurred in all the cases before convalescence had set in, but in some, probably in all, the fever was a long one; this feature, occurring in the second or third week of the disease, helped in two or three cases to determine the real nature of an otherwise indeterminate fever.

Passing next to the more strictly nervous phenomena of influenza we are confronted by the most bewildering as it is the most interesting feature of the disease. And surely of these the suddenness of onset is both the earliest and most striking. A medical man went to bed in his usual health, as he thought, and getting up during the night to void urine, he fell to the ground, and was so weak that he was unable to get into bed again without assistance. Another man was out in his dog-cart driving and quite well. He suddenly fell out insensible. He was picked up, got into the cart and drove himself home; but although he had broken a rib he remembers nothing about the drive, and when he arrived was so dazed that he wanted to get into bed with his boots on, and was thought to be intoxicated. Many similar and even more striking instances might be given of the extraordinary rapidity with which strong men were instantaneously laid low; but these must suffice.

Then there is the intense headache; the extreme prostration, quite out of proportion to the severity of the fever; the occasional maniacal delirium of the onset, or it may be, even definite symptoms of meningitis; the marked mental depression that marches with the disease or follows it. Neuralgia, too, is very common, sometimes mapping out the distribution of certain nerves, and followed by paralysis or other evidence of neuritis; sometimes attacking organs and producing, for example, pain in the eyeball, chest pang, nephralgia, neuralgia of the testis. Then there are the racking pains in the bones — pains indeed almost anywhere; subjective sensations of all sorts and in all parts, for this short summary is bald indeed in comparison with the multitudinous effects described by the many who were affected.

Of the disease as it spends itself upon the abdominal organs, it will suffice perhaps to say that in one of the later recrudescences of the 1889 to 1895 epidemic, there were a fair proportion of cases in which the chief symptom was of choleraic character — the attack being ushered in by a profuse watery diarrhœa. A gentleman who lived upon a well-appointed flat, and who, therefore, had everything handy to his convenience, related that his attack was so sudden, so urgent, and so profuse, that it

was impossible for him to retain his control over his sphincter, and that in the few yards between his room and the water-closet a stream of fluid poured from him. Dr. Simon of Birmingham has put on record (2) a series of similar cases, abdominal pain and collapse being added to the liquid discharges in true cholera fashion. Of other less common modes of onset it is less necessary to speak, for it is quite impossible to mention all the vagaries of the attack of this most searching disease; but I have heard of a series of cases all of which presented hæmaturia; and many cases have commenced with sore throat, or acute pain, swelling and abscess in the ear.

And now before dismissing the primary disease and passing on to conditions that may with some propriety be called sequelæ, there is good reason for taking the leading phenomena of the attack as here enumerated, and considering them a little more in detail.

Of the *suddenness of onset* enough has perhaps been said. It was so sudden in some cases as to be instantaneous, and the completeness of the prostration by which it not only, as it were, flung strong men down, but kept them down, was a thing that appears to be almost peculiar to the disease. Only in Cholera Asiatica is the collapse anything like so sudden and continuous, and herein it is due, perhaps, not so much to physical weakness as to retardation of the circulation and the mental hebetude entailed by it.

The *headache* was of an unusually severe character. Descriptions of it varied, but it was mostly frontal or orbital, and of that terrible kind that forbids sleep and goads the patient into delirium. It was very like the bad headache that ushers in many a case of typhoid fever; but it seldom lasted so long, and usually subsided after two or three days, often earlier.

The *aches and pains* in the bones and general soreness, in like manner, were very severe; sometimes they were like the pain of a breaking bone; sometimes they resembled not a little the lightning pains of tabes dorsalis; sometimes there was a more general ache and soreness in head, in shoulders, loins, thighs, that forbade ease in any position and gave rise to an indescribable unrest. Fortunately, as with the headache, the pains did not usually last in any severity over two or three days.

The appearance of the *tongue* was quite characteristic. With occasional exceptions, such as have been mentioned, it was tremulous, large, soft, indented by the teeth, moist, and uniformly coated with a thick, perhaps rather dirty, creamy fur. This was usually associated with a peculiarly offensive fetid odour of breath, which one cannot attempt to describe. Indeed, who should attempt to describe a smell unless there be an easily recognisable odour with which to compare it? The chief characteristic of this influenza smell was its overpowering nastiness. The odour of the sweat of influenza has also been described as peculiar —peppery, mousy, fusty, or mouldy (3).

Of the *pulse*, the most distinguishing characteristic seemed to me to

be that for the severity of the illness it seldom underwent any proportionate acceleration. A sharp fever with a pulse of only 80 or 90 was quite a usual occurrence.

Coryzal symptoms were sometimes severe, but they were not a predominant feature in this epidemic. Probably they were more often in evidence in the earlier part of the outbreak than in its later years.

The *cough* no less had features of its own. It was hard, dry, and racking. It did not ease itself by its occurrence. It often came on in violent paroxysms, suggestive, as some have said, of whooping-cough, and with the headache, often existing meanwhile, would give rise to the most intolerable disquiet. It was not accompanied by any expectoration to speak of, and it was exceedingly intractable to remedies. From one to another went the question — What is the best remedy for the cough of influenza? and the common experience seemed to be that no drug could be relied upon.

Passing next to the *fever*, it had no very definite type, and unless disturbed by any complication, pulmonary or other, it did not usually run to any unusual height. Its duration was variable; in many cases not more than three or four days; but in many also it would run ten or twelve, or even more. In not a few it ran the twenty-one-day fever of typhoid very close. It might be said by some that the fever was also very liable to relapse, but this would not perhaps be strictly true, for this relapse was almost always associated with the occurrence of some complication, even though, as I should certainly contend, such complications — pneumonia, for example — by their frequent occurrence showed themselves to be a part of the disease. It has been asked by some whether influenza is ever an apyrexial disease. There can be no doubt that it is so sometimes, as virulent forms of other infectious diseases may be. A lady in the height of one of the outbreaks came to feel so exceedingly ill that she was obliged to take to bed. She had excessive headache, and neuralgic pains in various parts of the body, and was ill for many days, and much depressed for some time afterwards. Her temperature was below normal all the time. My colleague, Dr. Wilks (4), records, amongst several others, the case of a gentleman, with whom he is well acquainted, who suffered severely, and was many weeks ill with influenza, yet who had no fever at any time. A very well-known and able practitioner of my acquaintance in the provinces even contends that "typical influenza" has no fever. It is not possible to accept such a statement of influenza in general, but it is possible that it may be true for a special locality or a special period of an outbreak. At any rate the observation is of importance as bearing upon the general question, and the point cannot be contested. And why should it be? Contagious diseases are by no means wanting which show a similar peculiarity. Cholera is one; but the most comparable is diphtheria, a disease mostly associated with pyrexia, but in which pyrexia may be quite absent, and that without allowing thereby of any more hopeful forecast. Any poison specially

noxious to the nerve centres may so alter the natural heat-regulating processes as to appear upon occasion as an apyrexial disease. That influenza is a malady that expends its force largely upon the nervous centres cannot at this date be denied, and it is equally certain that it may strike, and strike hard, and yet the sufferer be free from fever all the time [*vide* arts. on other Infections].

Another common and characteristic symptom, at any rate after two or three days had passed, was the occurrence of drenching *sweats*. They were variable in severity — to judge from the descriptions of the sufferers — from a peculiarly unpleasant feeling of cold down the back up to the most profuse sweats. Moreover, as with other features of the disease, they were very obstinate in their tendency to recurrence, and many were the cases in which this symptom outlasted all the others, and, indeed, only gradually died out after many weeks, or even months.

The occurrence of rigors is another characteristic that may be coupled with the sweats, because it emphasises the likeness of this disease to those of malarial origin — a likeness that has shown itself from the earliest days of the history of the disease when ague and influenza appear to have been considered in common. So far as my own experience goes, I think it may be said that hitherto, and until the occurrence of the late epidemic, those of the present generation were unfamiliar with severe and repeated rigors, except as the heralds of acute disease or of true ague, or of localised suppuration in this part or that, for example, in the cellular tissue or liver. But influenza introduced us to another common cause of rigors, and severe and repeated shiverings which, before 1889, would certainly have been taken to indicate the formation of pus, have now to be considered from a wider point of view. I have several times known of rigors so severe and so repeated, and the patient to be so ill, as to give the appearance and the subjective sensation of impending death; that one could not but surmise the case to be one of virulent septic poisoning, or of the local formation of pus; and yet, after provoking this diagnosis, the symptoms have disappeared again without any such untoward result. I have also known of three cases, at least, in which daily recurring rigors lasted over several weeks.

Yet one more symptom may be insisted upon, because I have repeatedly found it of value in diagnosis, namely, the extensive diffusion over the bases of the lungs of characteristic *sharp, sticky rales*. It is a pity that no verbal description can convey an idea of the peculiarity of this feature of the disease. It will occur to many that the bronchitis of typhoid cannot be very different, and yet any one familiar with the pulmonary sounds in the two diseases would surely bear out the statement that the two conditions are distinguishable by the ear. In typhoid fever the abnormal sounds are chiefly sibilant and musical wheezings, with no great amount of rale. In influenza the rales were of medium size, sharp in quality, and conveying the idea of a peculiar viscidity of the contents of the smaller bronchial tubes. And the

clinical course of the pulmonary affection was quite in accord with this presumption of the nature of the diseased product. For in many cases the mucus could not be expelled, and it was long before there was any expectoration. And for the same reason the lung was long in returning to its healthy state. In many cases, indeed, here was one of the chief dangers of the disease; the mischief crept from some small area at the base of one lung over a larger and larger area of that lung, and then to the other lung, without showing any sign of giving way: in not a few cases the patient was slowly choked by the spread of an exudation or secretion, with the formation or expectoration of which medicine was quite powerless to deal.

And now to pass to the **after effects of influenza**: I can hardly do better than set out with the words of a layman who, in describing its effects, said: "It hit me hard, for it ridged my nails." As with the initial symptoms of the disease, so with the sequelæ, the general prostration may well take precedence of any other more definite nerve lesions. For of all the complaints that are made there is certainly none more common than this: "I had the influenza, and have never been well since." It may be that the sufferer complains of frequent headache; but more often of a feeling of constant "good-for-nothingness," an everlasting sense of fatigue, both of body and mind: to move is an exertion that is almost insupportable, and is followed by profuse sweats; all power of sustained thought is gone. Dr. Gowers has well described this state of things. "It is," he says, "an intense feeling of inertia. Every action, physical or mental, requires an effort of the will to initiate and maintain it that is almost painful. Immobility of mind and body alone seem possible, and yet even rest has to be endured, for it brings no freedom from the sense of prostration. So strange and unfamiliar is the state that it seems at first as if it be only transient, and would be gone to-morrow; but the mistake is realised when day after day, week after week, pass without relief. In perhaps the majority it is only after some months that the natural freedom of untrammelled effort is regained." To this may be added that even now, five years after the original outbreak of this the latest epidemic, there are many who still suffer more or less from sensations such as are here described.

Again, frequent is the case where peculiar "all-overish" attacks have repeatedly seized the man or woman; sometimes flushings, sometimes indescribable internal sensations, but in all cases associated with such a dread or panic of impending death that, as several persons have told me, they would far sooner die outright and have done with it.

Of more definite disease of the nervous system I have myself seen several cases of temporary *mental aberration*, and Dr. Althaus has collected many cases of all kinds, from simple hypochondriasis to melancholia, mania, and general paralysis. Suicidal temptations seemed especially to follow influenza. Cases of this sort are observed after other severe febrile affections — typhoid fever, for instance — but after no one can it be said that such an occurrence is anything like so common as

has been our experience in influenza. But we are not dependent upon what may be called functional maladies such as these, for there have been cases of acute meningitis, for example, during the recent epidemic which have afforded presumptive evidence of being related to influenza. Or if such cases as these allow of doubt, there are other acute lesions of spinal cord and nerves which have been recorded in considerable number. *Neuralgia*, of one distribution or another, has been noted in any number of cases; and of still more serious lesions, Dr. Buzzard, in a later volume of this work, will record a case of acute *multiple neuritis* that came under the cognisance of Professor Clifford Allbutt and himself, which terminated fatally. Dr. Gowers alludes to cases of neuritis, and also to the curious circumstance that disturbances of sensation appear to be less common in this form than in that produced by other toxic agents. Dr. Gowers also notes that influenzal neuritis appears more prone to attack the face than other forms. A case is quoted from Westphal, where a man aged twenty-five, on the eighth day of convalescence from a sharp attack of influenza, found that his limbs were becoming weak. The loss of power rapidly increased, included all his limbs, and extended to both sides of his face. The nerve trunks and muscles of the trunk were tender, and the muscles quickly lost faradaic irritability, but preserved voltaic — the reaction characteristic of nerve degeneration. There was but slight disturbance of sensation. When the loss of power had reached a considerable degree it was accompanied by the peculiar œdema of the extremities, often met with in multiple neuritis. Then the palsy ceased to increase, and after two weeks more began to lessen — at first slowly, and then rapidly; and went on to complete recovery. Dr. Clifford Allbutt tells me of a case of peripheral neuritis of the lower extremities, in which the gait resembled a case of locomotor ataxy; the knee jerks however remained. I have myself seen two cases of paresis of the lower extremities associated with muscular wasting, and have seen or heard of many cases of local wasting of groups of muscles that indicated a localised neuritis. A very interesting group of this sort are the ophthalmoplegias. Of the external group the external recti appear to be the most often affected. Of internal ocular palsies loss of accommodation has been described, and is said by Althaus to be very common: this is one of the several points of resemblance between this disease and diphtheria. Many other ocular troubles have been described in influenza; chief of them is neuritis of the optic nerve or of its sheath, followed by optic atrophy and amaurosis. Ulceration of the cornea was not very uncommon (Higgens), and, in thus mentioning the loss of sight, one may link with it also a loss of smell sometimes complained of, and still more often a loss of taste that lingered long after the disease had subsided.

Besides these conditions changes have been recorded, both at home and abroad, that have not usually been attributed to any toxic agency such as we suppose this disease to be. Of these is *acute myelitis*, occasionally localised, but more usually disseminated through more

or less of the spinal cord. Even more chronic changes still are said to have followed it, such as locomotor ataxy, spastic paralysis, and so on. It is said that these serious lesions are more likely to occur in the later of repeated attacks than in the first, and it is certain that they bear no relation to the severity of the attack. The post-influenzal, like the post-diphtheritic nerve lesions, may be just as severe after mild as after severe attacks. Dr. Wilks, in respect of this very point, contends that we have no right to call many of these nervous phenomena "sequelæ," for, inasmuch as in many cases they are the only symptoms, they are the essential disease. As another sequela *diabetes* may next be mentioned, not because it has been common, but because of its nervous origin: Dr. Saundby has described post-influential diabetes, so also has Eischel, and I have seen a case. Sir T. Grainger Stewart asserts that a considerable number of cases took origin after influenza, and that in a considerable number of those already diabetic coma supervened as the result of the intercurrent malady.

Of the *pulmonary sequelæ* pneumonia was the most frequent. That it is, often, an integral part of the disease has already been said, but in many it was probably rather a sequela, the influenza bacillus being absent and the pneumococcus present. It is necessary, therefore, to suppose, as I shall presently say of typhoid fever, that the influenza in some cases laid its victim open to an attack of pneumonia.

In another large number of cases this seemed certainly true as regards pulmonary tuberculosis. Many a case seemed to start from an attack of influenza, and many a case of phthisis was certainly sent on its way with an alarming increase in the rapidity of its progress. Asthma, though in nothing like the same degree, is another malady that has in some cases been definitely traced to an attack of influenza; and in two instances I have known it to be the initial symptom of the epidemic disease. There is also no doubt, too, that empyema is unusually prone to follow upon the acute pulmonary inflammations that arise in influenza. Probably the same may be said of pyo-pericardium. I met with four cases in the height of the epidemic, and I shall also state my strong belief that *ulcerative endocarditis* was no uncommon outcome; at any rate it seemed to me to be disproportionately frequent during the epidemic. Quite recently a woman with mitral disease in Guy's Hospital took influenza, and thenceforward remained feverish and died after several weeks of malignant endocarditis with infarctions in the spleen and pneumonia.

The mention of unhealthy inflammations of this sort may well lead on to the next sequela that was very common, namely, the formation of *abscesses* in various parts of the body. Many were glandular abscesses, but not all. Abscesses in the brain, in the lungs, in and about joints, in the neck, axilla, groin, have all been met with, and, at one period of the epidemic, otitis of the middle ear and abscess following upon influenzal sore throat was quite a common occurrence. Suppuration in the antrum of Highmore is a distressing and possibly fatal sequela which for a time may escape diagnosis.

These are the main results of this strange and terrible disease. But the list is by no means exhausted. There would appear to be no organ or tissue that may not become the subject of its attack. Dr. Boulting tells me of four cases of *myxœdema* that he believes to have been consequences of attacks of influenza, and acute thyroiditis was twice recorded (in the *British Medical Journal*) during the year 1895 as a complication of influenza. *Purpura hæmorrhagica* deserves mention. Dr. Sansom has recorded a case associated with *acute pemphigus*, and Professor Allbutt tells me of another that occurred in a severe case of influenza with pneumonia and recurrent attacks of mild mania. The patient was a gentleman of forty-five, over the trunk of whose body, though chiefly towards the back whereon he lay, were very black, close set petechiæ, that took many weeks to fade. A variety of erythematous eruptions upon the skin have been noticed; and albuminuria and hæmaturia were not uncommon with *nephritis* as an occasional result. *Orchitis* has been noticed in one or two cases.

Lastly, one may notice the persistence, long after the disease has spent itself, of a *subnormal temperature*, a condition that may be taken to mean either the long-lasting influence of the disease upon the nervous centres, or no more than the dyspepsia, the neuralgia, the general "good-for-nothingness" which are expressive of the severity of the illness the sufferer has passed through. And in this regard may be mentioned two other curious results of the disease that are to be explained, one may suppose, in the same way: one is the development in some people of an *unnatural appetite*. A friend tells me that for a long time after the attack, though habitually a small eater, and taking next to no food in the middle of the day, he would eat four enormous meals; and if from stress of work he was unable to get food, he would suffer such intolerable agony in his stomach that he would rather have died. The other point is the toleration of alcohol that followed the disease in some persons. A young man told me that he was so weak after his attack that he daily took a quart of stout at his lunch and another at dinner, and "it never seemed to go anywhere," nor did he experience any ill effect. An old lady, who in ordinary circumstances was a small eater and seldom took alcohol in any form, had a mild attack of influenza and then a relapse with diffuse phlegmonous cellulitis of one leg. She now took food in large quantities, enough, it was said, for three men, so as to be the astonishment of her friends; and she took twenty-five ounces of brandy, two-thirds of a bottle of port, and a pint of champagne in the twenty-four hours for ten days or more consecutively and made a good recovery.

Etiology and Pathology. — It is a matter of doubt when the disease that we now call influenza first appeared in England. In the sixteenth and seventeenth centuries ague and influenza were not adequately distinguished. The notion of ague, as Creighton remarks, was uppermost, and there were no means of distinguishing one disease from the

other. In the eighteenth and nineteenth centuries the idea of catarrh has been the more prominent.

But it would seem probable that since 1650, or thereabouts, a disease of the same characters as our visitant of recent times, or approaching thereto, has now and again appeared in this country. This, however, would hardly be supposed from the various appellations given to it. Some of these, as narrated by Creighton, are as follows: In 1562, "the new acquaintance;" in 1580, "the gentle correction;" and at later dates "the new delight," "the jolly rant." There can be few indeed, having had experience of our recent epidemic, who would not rather subscribe to the propriety of the term "knock-me-down fever" (applied sometimes to dengue), than speak of it thus tenderly as "the gentle correction," and still less as "the new delight." Happy are we, if with our recent and vivid memory of such a scourge, we can yet smile at the conceits of a bygone day.

So far as the attack itself is concerned, the description of the epidemics of earlier times are wonderfully accurate now. Subjoined is a description by Huxham of the disease as it appeared to him in 1733 (5): "It began with slight shivering, followed by transient erratic heats, headache, violent sneezing, flying pains in the back and chest, violent cough, a running of thin, sharp mucus from the nose and mouth. A slight fever followed, with the pulse quick, but not hard or tense. The urine was thick and whitish, the sediment yellowish white, seldom red. Several had racking pain in the head, many had singing in the ears and pain in the meatus auditorius, where sometimes an abscess formed; ulcerations and swelling of the fauces were likewise very common. The sick were in general much given to sweating, which, when it broke out of its own accord and was very plentiful, continuing without striking in again, did often in the space of two or three days carry off the fever. The disorder in other cases terminated with a discharge of bilious matter by stool, and sometimes by the breaking forth of fiery pimples. It was rarely fatal, and then mostly to infants and old, worn-out people. Generally it went off about the fourth day, leaving a troublesome cough, often of long duration, and such dejection of strength as one would hardly have expected from the shortness of the time. The cough in all was very vehement, hardly to be subdued by anodynes; and it was so protracted in some as to throw them into consumption, which carried them off within a month or two."

This description, except in the statement that the disease is rarely fatal except to infants and old, worn-out people — and it is still emphatically true, that to the free liver and the aged the risk was largely increased — would include many of the main features of the disease now. Moreover, there are those still living who experienced an attack in the epidemic of 1847–48, and who having suffered again now, were able to identify their old enemy without any hesitation. Its prevalence has been that of sudden, sharp, short outbursts, mostly exhausting themselves after a few weeks of virulent fury, and then several recurrences

at longer or shorter intervals, until at last it has disappeared altogether for ten, twelve or twenty years. In times gone by the suddenness of its invasion, the rapid way in which numbers were attacked almost, one might say, at a definite hour, certainly upon a definite day, and the alleged fact that the disease attacked not only those on land, but also appeared upon ships far away from land, and therefore out of all possible contact with sources of contagion, have led to the belief that the disease is one that owns some atmospheric origin. But in the last attack the observation that has been brought to bear upon this point has made it certain that the incubation is very short, that the disease is contagious from man to man, that the contagion is carried about by fomites, and that it is by these means chiefly that the disease is spread. For instance, the invasion of a country or district when examined into is clearly not so sudden as has been thought. In the first outburst of the disease in the winter of 1889, the disorder befell us, apparently, almost upon a particular day in the last week in December. But, as I have already said, cases had occurred for several weeks before; and this is certainly true, for on looking over notes of cases at that period I find several in the preceding month or five weeks that puzzled me at the time, but which I know now to have been influenza. So also when the outbreaks on vessels far from land come to be inquired into, not one, in the opinion of Dr. Parsons, is free from the suspicion that there may have been less complete isolation than has been currently reported. Again, the few towns or villages that have escaped have been remarkable for remoteness of situation or natural inaccessibility, curtailing, therefore, within the narrowest possible limits the intercourse between those within and those beyond their borders. On the other hand, in instances too numerous to mention, the disease has apparently started and spread rapidly from the date of a person going from an infected area to either a healthy house, village, or public institution.

The permanent home of influenza, if one there be, is not yet absolutely certain. The west of Russia seems on the whole to be its most likely source, for it would appear that "La Grippe" figures largely as a disease in Russia in ordinary years (6). It has been thought by some that the disease is really dengue fever under another name, but this cannot be. The two diseases are no doubt strikingly alike in some general features, but there are also striking differences (*vide* art. on "Dengue"). The natural habitat is an important one. Influenza seems to spare no climate, whereas dengue is a disease of hot seasons only. There are regions, again, where outbreaks of the one and the other have followed each other at such short intervals (3) that if the one disease has offered no protection against the other the occasion has yet offered an opportunity for skilled observers to watch the one disease with the other fresh in memory, and to contrast the two. Perhaps the most marked difference between the two is that dengue is almost invariably associated with a rash, and is often followed by desquamation in large flakes, whilst influenza is but rarely accompanied by an eruption.

The incubation is probably short. From two to five days is apparently the limit: usually two or three days, though this cannot be said to be substantiated with any degree of certainty, and a still shorter period has been alleged. Not only is the incubation short, but the infective power of the disease develops early, as might be expected from a disorder so distinctly catarrhal in character; for a like reason it is not surprising that instances are on record where the infective power appears to have remained for many days after the onset of the affection. It is obvious that if the infective agent be largely present in the bronchial secretion as well as in that of the nasal passages, the duration of possible infective power might need to be measured by the continuance of the catarrh, whether it relapse in the particular case or not. In this respect it may be that pertussis and influenza show a resemblance to each other. In making this comparison, however, it is necessary to remember that pertussis is prone to relapse again and again long after the primary disease, and that there is no evidence that the relapses are infective in their nature. It may perhaps be thus with influenza — at any rate in those common cases in which certain individuals are said to have had the disease time after time.

The shortness of incubation and early activity of the infecting agent are of paramount importance when considering the next question, namely, the epidemic character of the disease. A short period of incubation must enormously increase the rapidity of the spread of any disease that is contagious. But scarlatina is a disease that has a similar period of incubation, and no such sudden outbreaks are known with it. But two important qualifications have to be considered in this comparison. In the first place, scarlatina exhausts the soil and protects its subject against recurrence; secondly, it is more or less always with us. Influenza does not render its subjects immune — not, at any rate, to anything like the same extent, certain persons seem indeed to be attacked, preferentially, as it were, again and again — and even allowing that, as some insist, the catarrhal conditions that are more or less always present at certain seasons are influenza *in posse*, influenza cannot be said to be always with us in any such sense as is scarlatina. It may be asserted, then, that influenza when it comes finds a soil prone to it instead of proof against it, and finds such conditions over a very wide area of the earth's surface. No previous epidemics have prepared man to resist it in any way, even if they have such a power; like a familiar guest, it finds us with open house everywhere. And if to such ready access be added the other factor that, like measles, it infects actively so early that it is at work for this purpose long before it can be recognised, we have a combination of circumstances that, as Dr. Parsons insists, explains the extraordinary rapidity of the diffusion of the disease, and one that must be carefully considered and appraised before any attempt be made to estimate the nature or the power of epidemic influence.

What additional influence or influences make for an epidemic are still unknown. It cannot be doubted that some such are needed, and

that, speaking generally, they must be of atmospheric order. We have knowledge of epidemics of voles, of locusts, of wasps, of certain caterpillars, of the Colorado beetle, of certain blights, depending no doubt upon the conditions of environment of these lower orders of life by which their reproduction has been extraordinarily facilitated. There seems no adequate reason against some assumption of the kind in the present case. Short incubation, early activity of infecting power, and absence of immunity, would all seem to forecast an endemic rather than an epidemic disease; whereas influenza sweeps over the world and it is gone. We can see it afar off, and trace its progress, but can do nothing to stop it; and it smites the sanitarily pure with a severity on the whole much the same as it shows to the rest of the world.

Atmospheric influences no doubt vary considerably within limits, else why should some suffer headache when thunder is in the air, or the corns of others shoot when dry weather breaks into wet? And as in all zymotic diseases, even endemic ones, there are times when the disease is violently active, times when it sleeps and seems almost to disappear, the conditions of its life history remaining constant all the time, there is no need to labour the proof of epidemicity. We know nothing whatever, and are a long way off the discovery of subtle influences of this kind, but none the less they certainly exist.

The main point, however, that has been made in the present epidemic is that the influenza is contagious; this being so, it becomes probable that it is of microbic origin, and investigations in pursuit of a specific germ have resulted in the discovery of a bacillus that has distinguishing characteristics. This bacillus, according to Klein, was first found by Canon, and being found in the blood was supposed by him to cause the symptoms by circulating in that medium. But so many subsequent observers have failed either to cultivate the germ or to produce the disease by inoculation, that Dr. Klein suggests that such bacilli as are found in the blood are mostly dead. Pfeiffer about the same time described the influenza bacillus independently of Canon, and stated that the home of the active germ is in the gray mucus of the respiratory tract, where the bacilli exist in such numbers, that by care in selecting the specimen almost a pure culture may be obtained. This is corroborated by Kitasato and others.

As regards cultivation of the bacillus, Pfeiffer has produced by inoculation in monkeys symptoms similar to those of influenza. Dr. Klein (7) has made numerous experiments by inoculation of the pure culture upon rabbits and monkeys; in only one monkey was any success obtained, but the juices from this animal when injected into other monkeys produced the disease in some of them. This difficulty of reproducing the disease by inoculation is of importance, because it is believed by some that human influenza exists also in horses, dogs, and cats. There is some evidence in support of the belief, but it is meagre and equivocal.

Pfeiffer's bacillus, as it is now called, is very minute — 0·4 m. in thickness, 0·8 m. in length (7). It occurs in masses, or singly, or in twos and

threes. In stained specimens it has a peculiar appearance, the protoplasm being segregated into a stained granule at each end, while the middle portion remains unstained, and shows only the outline of the sheath. Thus the bacillus looks like a diplococcus, and where two are placed end to end, they look like a chain streptococcus of four spherical cocci. They are found in quantities in the bronchial secretion, and, in severe cases, in the peribronchial and subpleural lymphatics.

The bacillus stains with difficulty. My colleague, Dr. Washbourn, to whom the three foregoing paragraphs have been submitted, states that the best method is to use a solution of carbolic fuchsin diluted with water. The smeared cover-glass is dried and then stained for ten minutes, afterwards washed with water, dried, and mounted in the usual way. The cultivation of the bacillus, a matter of some difficulty, is favoured by the presence of hæmoglobin in the medium. The best method is to remove blood from the blood-vessels of pigeons with aseptic precautions, and allow it to clot upon the surface of agar sterilised in a test-tube. The sputum is sown upon the surface of the blood, and the tube kept in an incubator at blood heat for twenty-four hours. By this time the influenza bacilli will have formed minute transparent colonies hardly visible to the naked eye. This bacillus is characteristic of the disease. So far it has not been discovered in the blood or secretions from patients suffering from other diseases.

Thus much of the bacillus. It is consistent with all that is known of most of these minute organisms that their presence in the secretions of one part or another should be associated with a specific state of pyrexia in the individual attacked. But we have yet to consider the relation of the germ to the after effects of the disease, and the explanation of these is by no means free from difficulty. Influenza in its sudden and severe prostration is very like typhus fever; in its disturbance of the nervous centres and tracts it is more like diphtheria. The difficulty in both is that the after effects may come on when and indeed long after the primary disease appears to have spent itself. Up till recent times no explanation of this phenomenon has been at all satisfactory; but now the theory of the production of toxins during the growth of the bacillus adapts itself reasonably and it would seem adequately to the peculiar explanations of such cases. Upon this hypothesis the life and growth of the bacillus leads to the production of poisonous material in the juices upon which it thrives: this is carried into the circulation, and gradually works out the distributed effects which characterise the sequelæ of each.

Morbid Anatomy. — The mortality of influenza was so large that much information might have been expected under this head. But indeed our knowledge has not been greatly extended. In all sudden epidemics of the kind the disease is so distributed that comparatively few deaths occur in public institutions where such opportunities can be utilised; moreover, the outbreaks are so overwhelming that it is impossible to

turn aside from the living to the dead. Indeed we have not yet arrived at that certainty which will enable us always to distinguish between the changes in tissues or organs that are due to this acute process or the other.

Thus, speaking generally, the changes in the lung, for example, are those of bronchopneumonia, of acute lobar pneumonia, or of acute bronchitis; yet there are no obvious morbid characters by which, apart from the history of the case, we can recognise such changes as belonging to influenza. It is true in the main that the morbid changes of influenza are the result of certain secondary processes: influenza opens the door, as it were, to various other poisons, which we have already indicated in the clinical description — the streptococcus with the consequent production of pus, the pneumococcus with the production of pneumonia, and so on.

Certain changes, which appear to be peculiar, have, however, been described in the lungs, not only in the more recent, but also in several of the earlier visitations. I may quote, in particular, from an account of the epidemic of 1837, as recorded by Graves upon the authority of Dr. George Green: "The bronchial mucous membrane was found in every case more or less congested and inflamed. . . . The inflammation in most cases occupied the trachea and the bronchial tubes of both lungs. . . . A sanguinolent frothy mucus occupied the area of the tubes, and increased in quantity as they were traced to their minuter divisions. The parenchymatous tissue of the lung was invariably discoloured, and it did not crepitate, or very feebly so, when pressed between the fingers. The surface of its section was not rough to the touch, and when pressed in the hand a quantity of the mucus described was driven out. . . . When the torn surface of such lungs was examined it did not appear granulated. . . . The signs of recent pleuritis were rare."

Dr. Louis Hayne, writing of the morbid anatomy of the lungs in the recent epidemics (11), agrees very closely with this description. He notes the frequency of lobar pneumonia and its tendency to attack the upper lobe. Dr. Ribbert of Berlin is quoted to the effect that "the hepatisation on section has a peculiarly smooth aspect, differing from the ordinary granular aspect of acute croupous pneumonia. Sometimes there is marked interstitial inflammation, explaining perhaps the tendency to abscess and pulmonary gangrene. This peculiar smooth aspect has been frequently observed in the deaths from recent epidemics, as has also the association with it of areas of bronchopneumonia. Often the solid lung looks as though it were composed of a number of patches of bronchopneumonic consolidation, these patches having run together and involved the whole lung, suggesting the appearance of a confluent bronchopneumonia rather than that of the croupous variety of pneumonia. . . . This is often found in conjunction with red hepatisation. . . . In some cases pale patches of bronchopneumonia are scattered throughout the lung so as to suggest at first sight the existence of miliary tubercle. As regards the bronchi, inflammation of the larger tubes is very common, besides the

capillary bronchitis, the bronchi being congested and covered with thick mucus. The tubes are generally filled even to considerable dilatation with muco-pus. The whole thickness of the bronchial wall is softened. Sometimes the contents of the bronchial tubes are not mucopurulent, but fibrinous."

I cannot myself attribute much significance to this smoothness of surface. I am quite familiar with it as, at any rate, an occasional feature of irregular forms of pneumonia; and it has seemed to me sometimes to be due to a want of intensity in the exudative process, sometimes to the occurrence of mixed forms of inflammation, particularly in the direction of interstitial changes and nuclear proliferation, associated with collapse of the spongy structure of the lung.

Little more can be said, and this little is scarcely distinctive. Probably as much could be said of an epidemic of measles. The peculiarity of the changes lies mostly in the fact that acute bronchopneumonia, a rare disease in the adult, is the common morbid change found in the bodies of those who die of influenza, but that it is often associated with patches in which the microscopical changes are those of lobar pneumonia.

Before now quitting the etiology and pathology of the disease, I am tempted to say that epidemic disease has a valuable bearing upon a very interesting question, namely, that of the "change of type" of disease.

In diseases that are ever with us, that grow old as we do and with us, it is difficult, though it might seem easy, to express any opinion upon such a point. For it may easily be with disease as it is with the face of a familiar friend. How easy it is to think that face has altered in little or nothing since the days of our boyhood together! Yet what havoc does the fashion of the day, with its photographs of the individual at various stages of his existence, make with any such fond idea! In influenza, however, we have a disease which only visits us at considerable intervals, and thus it affords a favourable opportunity of eliminating this possible source of fallacy; and it would appear from evidence already quoted that there is no material alteration in the symptoms; as they were in former times, so they are now.

But it is possible that if the causes be the same the individual may have altered. Is there any evidence upon this head? Without answering this question in any decisive way, it may be worth while to point out that there is no record in former times of the long series of post-influenzal nerve disorders with which we are now but too familiar, and which will be found by our successors when in the heat of epidemics yet to come they study as we do to-day the recorded experience of the past. The difference in this respect that can be noticed between the past and present may indeed be due to a simple imperfection in the medical record, and the question must be left an open one; but it may well be considered a chief object of the chronicle of to-day to put clearly on record, that as a disease influenza has shattered the nervous systems of a large number of its victims, in some

cases permanently, in many for several years after it has run its course.

Whether this disorder has the power of modifying the course of other diseases may more conveniently be considered under the head of diagnosis now to come.

Diagnosis. — The general symptoms have already been sufficiently considered. All observers have insisted upon the extreme prostration as the typical feature of this disease. This has probably led us into some neglect of one or two other features that are probably not less weighty as means of diagnosis. Chief of these I would place the thick coating of a moist, dirty, creamy material upon a large, flabby, and often tremulous tongue. To this characteristic tongue must be added the tendency to profuse sweats, a pulse but little accelerated, and a pyrexia, if present, of indefinite type. In the great majority of cases the key to the diagnosis rested upon the accurate fitting or otherwise of one or other of these pieces into the mosaic — in such, at any rate, as presented any difficulty; and these were many. Any number of cases have been seen that at their onset looked like influenza, but which afterwards proved to be typhoid fever; and who can wonder that the diagnosis is occasionally a halting one? A large number of cases may each begin with headache, shivering, general aching, and a pulse but little above the natural rate. Sometimes, too, the spleen may be enlarged. How can the two diseases then be distinguished until some characteristic development occur? Watson noticed the resemblance of the early stages of influenza to continued fever. Yet it is possible that a provisional diagnosis of influenza and a final one of typhoid fever was by no means always a mere mistake; and there are those who think that the occurrence of the one disease lays the patient open to an attack of the other. Such proclivities are well recognised between measles and pertussis; between scarlatina and diphtheria. It may be so here, although where mistake is so easy it might seem unnecessary to apply any such disputable hypothesis. There is, however, the more reason for thinking this to be possible, as there seems some small amount of evidence that influenza, or the conditions of our environment that favour its development, may also modify in various ways the natural course of other diseases. Some examples of this tendency have already been alluded to, namely, the rapid development of pulmonary tuberculosis after influenza, the risk of pleurisy taking on a suppurative form, of an endocarditis assuming a malignant type, of a sore throat leading to an acute suppuration of the internal ear; and I cannot but think that typhoid fever has of late shown anomalous features that may possibly bear a similar interpretation. For example, a young man had been exposed to cold and wet during the prevalence of influenza, and had imperfectly guarded himself against such influences. He was seized with rigors and went to bed, and thenceforth his sole complaint — for he was quite clear in his mind — was that he was constantly drenched with perspiration. His temperature was 104°, his pulse only 90, his tongue moist and rather creamy, his bowels required some mild laxative.

Clearly the disease, although undoubtedly typhoid fever, for he had profuse intestinal hæmorrhage about the twelfth day, from which he rapidly sank, was, in respect of the rigors and sweating, of an influenzal type. Of late there have been many such cases of typhoid fever associated with inordinate sweating. Another case that I have some knowledge of began with wild maniacal delirium, much more like influenza than typhoid; and other examples could be given where premonitory symptoms of influenza ushered in typhoid fever, and this would seem to be a new experience. That this is no more than a personal opinion I fully admit, but even the opinions of those who have lived through an epidemic of a disease that may not visit us again for many years are worth mention. They must be recorded now or not at all, and they may be useful in the future as suggestions for observation and inquiry.

But difficulties of diagnosis arise in other directions. I well remember seeing a lady who was suffering severe and repeated rigors, which, together with high fever, seemed ominously indicative of hepatic abscess, or some internal source of grave septicæmia. She had undergone, a few weeks before, some slight operation upon the uterus, but was supposed to have quite recovered, and, as it proved, had recovered. Had it not been for the late epidemic of influenza which has enlarged our breadth of view in the matter of rigors, the diagnosis would have been unhesitatingly of a very grave character. As it was it remained doubtful, and the doubt was solved by the patient convalescing without a drawback of any kind.

One other point may be mentioned, namely, that influenza is often so indefinite in its features that the diagnosis can only be arrived at after the event, if then. And it is probable that this is of importance if any adequate notion of the impact of the disease upon the population is to be obtained. Here is an illustration of the sort of case that was constantly occurring. One member of a family had a sharp, febrile attack of quite indefinite nature. Within a few days another member had earache and double otitis; and then another had otitis, or a threatening of it, and mastoid pain, and this was followed by a troublesome orbital neuralgia. Taking the cases separately there is nothing to justify such a diagnosis, but putting them together, and bearing in mind the intimate relation that exists between influenza and inflammation of the internal ear, it is surely not improbable that the disorder in each case was influenza. To take another case: a man, apparently in perfect health, and having committed no indiscretion in diet that could by any means explain it, awakes in the middle of the night with indigestion and diarrhœa. The diarrhœa was a pure watery flux, was associated with slight pyrexia, lasted forty-eight hours, and left the man well but, for him, unusually limp and tired. There was no thought whatever of influenza. But, nevertheless, for weeks afterwards he was much troubled with an evening neuralgia of one side of the face; and not long afterwards, after a little excess of work and exposure that under ordinary circumstances would not have done any harm, he was seized again with a bad neuralgia, that woke him regularly for several

nights out of his first sleep and compelled him to sit up for the rest of the night. There is surely some ground for suspicion that the initial attack of choleraic diarrhœa was of influenzal nature, and that the neuralgia afterwards was the sequela that made the diagnosis possible.

Two other aspects remain to be considered, namely, prophylaxis and treatment, and these, though the most important of all, unhappily allow of a very brief statement.

As regards **prophylaxis,** the obvious thing is to keep out of the way of contagion. Where strict isolation has been possible, as in certain institutions, the disease has seldom appeared; most risk of catching the disease is run in public buildings or ill-ventilated rooms of any sort, a railway carriage with closed windows not excepted. It also seems certain that excesses in living of all kinds favoured the inroads of the disease, as also did exposure and fatigue. All observers have testified to the frequency of the disease and to its heavy mortality in the alcoholic particularly, and also in the overworked and harassed.

A large section of the public, in addition to common sense hygiene of this sort, applied itself to various drugs and inhalations in the hope of warding off an attack. Quinine was in most frequent demand internally, and eucalyptus as an inhalation; but it cannot be said that either quinine or salicin in the one way, or inhalation in the other, showed any positive success.

We are as yet in ignorance how long the influenzal poison retains its vitality, but common prudence suggests that infected rooms and clothing should be well disinfected after they have been contaminated.

Treatment. — There is no specific yet at hand for this disease. This is quite certain from the number of drugs that have been regarded as almost infallible by one observer and another. All are agreed, however, that mildness of attack and speedy recovery are best insured by taking at once to bed, and that it is the worst folly to struggle on with work and to attempt to fight the disease. — a plan that, although some came through successfully, was nevertheless the cause of the loss of many lives.

To go to bed, to take plenty of light liquid nourishment and some liquor ammoniæ acetatis every few hours, was sufficient in most cases to induce a quick recovery. Other remedies largely in request were salicylate of soda in ten grain doses every three or four hours, antipyrine, alone or combined with the former, phenacetin and quinine. Upon a review of the whole epidemic, there appears in these drugs nothing of a specific effect in cutting short the disease; but in many cases, by their sudorific action and in the control that these drugs have over the temperature, they were productive of relief, and made for the return of health. For the rest it is necessary to combat symptoms as may seem best: the cough perhaps most readily with opium in some form; the aches and pains perhaps in a similar manner; and for the long-lasting after effects some of the many good nerve tonics, and the judicious use of alcohol, have been upon the whole the most successful.

For most of the statements in the foregoing article I have appealed, in the first instance, to my own experience. But in the preparation of the article I have frequently referred to Dr. Theophilus Thomson's *Annals of Influenza in Great Britain from* 1510–1837; to the *Report to the Privy Council on Influenza* by Dr. Parsons; to the *Further Report and Papers on Epidemic Influenza*, 1889–92, by the same gentleman; to Dr. Klein's report in this latter volume; to a Monograph on Influenza by Dr. Althaus; and to Dr. Creighton's recently published *History of Epidemics in Britain*.

The literature of influenza scattered over the periodicals of the last few years is very voluminous; this also has been consulted as much as possible, but the task has been rendered incomparably lighter by such recent publications as those I have specially mentioned, containing as they practically do all the information that is to be obtained upon epidemic influenza.

J. F. Goodhart.

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J. F. G.

DIPHTHERIA[1]

Diphtheritis and Diphtheria are names which were invented by Bretonneau,[2] in 1821, to denote a certain kind of specific inflammation (*phlegmasie spécifique*). In his endeavours to distinguish diphtheria from other diseases he was compelled to rely altogether upon observations made at the bedside and post-mortem table; nor has any other means of discrimination been possible until within the last few years. Yet the clinical definition has never been adequate to its intention, and, in respect of some cases of sore throat attended by the formation of false membranes, it has always been doubtful hitherto whether they are to be deemed diphtheritic or not. At one time it seemed probable that an

[1] The history of diphtheria being beyond the scope of this essay, the reader may be referred to the works (1, 2, 3) mentioned at the end of it.

[2] "Il me soit permis de désigner cette phlegmasie par la dénomination de DIPHTHÉRITE, dérivé de ΔΙΦΘΕΡΑ, *pellis, exuvium, vestis coriacea*" (4), p. 41. (Διφθερίτης and διφθερίας have the same meaning: qui gestat pelliceam seu coriaceam tunicam.)

adequate definition, based upon the essential cause of the disease (the very *ens diphtheriæ*), could at length be propounded; that diphtheria might be taken to signify disease due to infection by the bacillus of Klebs.[1] But now we are told that the bacillus of Klebs and Löffler is not found in some of the cases which we have been accustomed to call diphtheritic, and that certain micrococci have the power of setting up a pellicular inflammation. So, if we continue to use the word diphtheria in the sense of Bretonneau, we must distinguish several kinds of that disease (bacillary, micrococcal and so forth); or if we restrict the use of the word to those cases in which the bacillus is found, we must invent new words to signify the other forms of pellicular sore throat. It would probably be the better course not to diminish the extent of meaning of the word diphtheria, and still to use it as Bretonneau used it, but in a generic sense. However, the popular tendency seems to be strongly in the other direction, that is to say, to confine the name to those cases in which the bacillus is found. Moreover, causes seldom operate singly and simply; and even that diphtheria which is characterised by the presence of the aforesaid bacillus, is so complicated by the action or co-operation of other morbific microbes, that diphtheria is seldom or never due to a simple infection. Nor has skill in bacteriological research yet come to be a usual accomplishment of medical men; hence the uncertainty concerning the nature of some kinds of sore throat, which has always prevailed, is far from wholly dispelled. Indeed, for practising physicians, the main note of diphtheria is still found in the presence, not of special microbes and morbid poisons, but of false membranes upon certain mucous surfaces or upon abraded skin; it being well understood that false membranes are not quite peculiar to diphtheria, even when that word is used in its most extensive sense: the mucous surfaces referred to are those of the throat, nose, and windpipe — not to speak of surfaces seldom affected, such as those of the stomach, conjunctiva and vulva. Definitions of this kind, though rude and inadequate, serve useful purposes until wrought out into a full description of the disease.

S. G.

Etiology and Prophylaxis. — There is much to justify Oertel's assertion that diphtheria is "one of the oldest epidemic diseases of the human race." A disease, in description like diphtheria, has prevailed from time to time in various parts of England. It occurred, mainly in a sporadic form, at intervals during the earlier half of the present century; it assumed an epidemic form when the "Boulogne sore-throat" occurred on the French coast; and from 1855 onwards the disease has been more

[1] In a book called *Scrutinium physico-medicum contagiosæ luis quæ dicitur Pestis*, by Athanasius Kircher, published in 1659, will be found a remarkable exposition of the doctrine that contagious diseases are dependent upon living particles, contagia viva, semina animata. He frequently refers to *male in canna* (diphtheria) as a kind of pestilence. Pestilential "effluvium est animata fœtura vermium. Sunt autem hi vermiculi pestis propagatores tam exigui, tam tenues et subtiles, ut omnem sensus captum eludant, nec non nisi exquisitissimo smicroscopio sub sensum cadant, atomos diceres."

or less continuously present in this country. Until recent days available statistics of diphtheria in England and Wales have been limited to fatal attacks; and most of the data, especially the earlier ones, are more or less imperfect by reason of faulty diagnosis and faulty nomenclature. But, such as they are, they show that during the three decennial periods, 1861–70, 1871–80, and 1881–90, the rates of mortality from diphtheria per million living were 187, 121, and 163 respectively. The increase of the rate of mortality from diphtheria indicated in 1881–90 has been more than maintained. In the eighteen years 1871–88, the mean of the annual diphtheria death-rates per million living in England and Wales had been 137, the rate hardly ever exceeding 160; but for the five years 1889–93 the mean of the rates has been 216, the rates for 1892 and 1893 being the highest ever recorded, namely, 222 and 318 respectively. Indeed, examination of the mortality returns shows that we are face to face with the fact that for a period of some twenty years there has been in England an increasing mortality from diphtheria, and that this increase has been specially marked during the more recent years of that period. To some extent this increase may be set down to improved diagnosis, and better methods for the certification of deaths; but no such explanation can account for an addition to the death-roll which, to use the description of the Registrar-General, must be regarded as "formidable." In studying the etiology of diphtheria account will be taken of this growing mortality from the disease; the more because there is ample evidence to show that diphtheria has not merely increased in fatality — whilst the total amount of sickness from that cause remains much as before — but that the increase in the number of diphtheria deaths has gone hand in hand with a wider diffusion of the disease throughout the country.

It may be convenient at this stage definitely to formulate *certain propositions respecting diphtheria* which I consider to be demonstrated. It does not fall to me to give proof of their truth; but in that which follows they must be constantly borne in mind by any one seeking to apprehend the etiology of the disease.

1. Diphtheria is a specific infectious disease, primarily and preferentially affecting mucous surfaces, notably the upper portion of the respiratory and alimentary mucous tracts; also, but more rarely, affecting abraded surfaces of the skin.

2. Diphtheria appears first as a local disease, the part attacked being the seat of an inflammatory process characterised by the formation of a false membranous deposit. The system as a whole is secondarily affected, the general disease being a sequence of the local one.

3. Local diphtheria results from the reception at a particular point of the mucous membrane and the subsequent development there of a definite micro-organism — the Klebs-Löffler *bacillus diphtheriæ*. This micro-organism, which is vegetable rather than animal in its nature must therefore be regarded as the particulate and essential cause of the local disease. The general symptoms of diphtheria, on the other hand,

are largely due to absorption into the system of a chemical poison or toxin, a result of the life-processes of the bacillus.

4. Diphtheria, or a disease *ejusdem generis*, is found in certain of the lower animals, and can be communicated to them from the human subject.

Consideration of the factors which favour diphtheria will involve reference to much that is still obscure; but our present knowledge of the etiology of the disease may best be set out by considering the character of the evidence on which certain conditions have been regarded as disposing to this disease.

Topography, Soil, etc. — It has been shown by Dr. Longstaff that, during the twenty-six years 1855–80, the greatest incidence of death from disease registered as diphtheria in this country took place on our eastern coast, namely, in Lincolnshire, Norfolk, Sussex, and North Yorks; that next in order came East York, Extra-Metropolitan Kent, and Essex, counties which are also on our eastern coast, together with Wales and certain counties within or bordering upon the Midlands; whereas the smallest death-rates from disease thus registered were recorded in Lancashire, Devon, and Somerset on the one hand, and in inland counties such as Bucks, Herts, Northampton, Leicester, and Gloucester on the other. These data in themselves, apart from other considerations, afford no sufficient indication that one or other portion of England is especially liable to fatal diphtheria; but when they are considered in connection with conditions of soil, surface, aspect and rainfall, there is some ground for believing that areas which favour retention in the soil of wetness and of dead organic matter, and are exposed to the influence of cold wet winds, do tend to the fostering and fatality of diphtheria. But that there are other conditions of equal if not of greater importance is unquestionable; indeed, there are already indications that the localisation of the diphtheria mortality, which Dr. Longstaff referred to as holding good up to 1880, has, by reason of other and more potent influences, undergone modification since that date.

Season. — It is generally admitted that, although diphtheria is now never absent from this country, season exerts a marked influence on its behaviour. Taking this country as a whole, the death records over a series of years show that the second quarter of the year exhibits the smallest number of fatal attacks; that there is some increase in the third quarter; that a very substantial addition to the number of deaths takes place in the fourth quarter, when the rate of mortality is at its highest; and that during the first quarter of the year, which ranks second as regards amount of death, a diminution in mortality sets in. Thus, during the twenty-four years 1870–93, the average annual number of deaths registered as diphtheria in England and Wales was distributed as follows: 1st quarter 1000, 2nd quarter 819, 3rd quarter 847, 4th quarter 1192. But, judging from available material concerning attack, non-fatal and fatal, it would appear that the increase in the mortality at the beginning of the fourth quarter is due to increase of attacks in

September; and that a not inconsiderable amount of death registered in the first quarter of the year relates to attacks which date from the latter part of the preceding quarter. In short, an increase of diphtheria commonly begins about the second or third week in September; the increase goes on augmenting through October and the greater part of November, and a decline in its amount usually sets in not later than mid-December. According to Mr. W. H. Power, October and November constitute "the well-known season of normal extra activity of diphtheria." There is a second tendency to exacerbation, on a much smaller scale, in the spring, commonly about the end of March or the beginning of April; after this the disease gradually falls to its minimum in June, July, or even in early August.

Sex and Age. — There is some excess of diphtheria in the female sex, but it would appear to be largely due to the greater opportunities of infection in girls and women than in the case of males. The excess in females commences at the age when little girls begin to tend the baby and younger children, whilst their brothers are occupied out of doors; and it is maintained throughout that period of life when women and mothers are engaged in house duties and in caring for the sick. Amongst females also habits, such as that of kissing, prevail to an extent which may account for some excess of a disease that is often conveyed from mouth to mouth. At the extremes of life the rate of diphtheria death in females does not exceed that in males.

The influence of age on diphtheria is very marked, whether death or attack be in question. By far the largest rate of mortality takes place during the first five years of life, and especially during the age-period 2 to 5 years; the period 5 to 10 years ranks next, and it is not till after the termination of the period 10 to 15 years that any substantial diminution sets in. In adult life and in old age the diphtheria death-rate is comparatively insignificant. With regard to the comparative immunity of infants under one year of age from death by diphtheria, it has been pointed out by Dr. D. A. Gresswell, now chief health officer to the Victorian Government, that infants at times suffer from diphtheria deposits in the fauces without obvious inconvenience, and that this may be due to the rudimentary character of the tonsils at that age. Speaking generally, and including non-fatal with fatal attacks, it may be asserted there is a special incident of diphtheria on the age-period 3 to 12 years. Now it will be at once remembered that the age 3 to 12 years is precisely that during which children are in attendance at the elementary schools.

School Influence. — The influence of school attendance on the diffusion of diphtheria was noted almost as soon as skilled inquiry into the circumstances of this disease was instituted. This was pointed out by Mr. W. H. Power in 1876, and in the following year I had an opportunity of studying the matter during a maintained prevalence of diphtheria at Coggeshall in Essex. It was found practicable to divide the 928 children in the village into age-groups, and then to ascertain within each group the

relative amount of diphtheria in those who attended school, and in those who did not. Under three years of age school attendance was not found to have materially influenced the number of attacks; but in the age-period 3 to 12 years the incidence of the disease was not far from 50 per cent greater on school attendants than on others; and in the age-period 12 to 15 years the school attendants suffered nearly three times more than those who were not at school. The same result was noted by other observers; and, quite apart from age susceptibility, it soon became evident that, there were certain circumstances associated with school attendance which promoted diphtheria. Indeed, this is now so generally accepted that restrictions in school attendance often form one of the earliest, if not the chief of the measures adopted by local authorities to prevent the diffusion of the disease. But as the subject was more carefully studied, it became evident that the influence of school attendance was by no means the simple affair of personal infection under circumstances especially favourable to the transfer of infection from one child to another; and another stage was reached when Mr. W. H. Power investigated a maintained prevalence of diphtheria at Pirbright in Surrey. School attendances were recognised there as serving to diffuse the malady amongst a somewhat scattered population; indeed, in hitherto uninfected households, children between three and twelve years of age, who at a given period were attending school, became affected five or six times as numerously as children of the same age who at the same period were not attending school. Hence, it was deemed desirable to close the schools on several occasions. It was also seen that attacks of "sore throat," which did not present the typical signs of diphtheria, and seemed often but trivial in their character, served as links between the more marked outbreaks of the disease. Hence, besides resort to measures of disinfection at the school-house and in invaded houses, sustained medical effort was made to eliminate from the school, on the occasion of each of its reopenings, all cases of sore throat, however mild. Thus it came about that comparison was possible between nine alternating periods of school work and school closure, — the intervals of closure lasting generally for some six weeks, and school operations not being recommenced until all signs of sore throat had disappeared amongst the scholars. "While the school remained open," writes Mr. Power, "in the early months of the year, the rate of attack in children aged from three to twelve, presumably susceptible of diphtheria, but not having the disease at home, was 16·6 per cent of those who were at school, and 3·8 per cent of those who were not. The next time the school was opened the respective rates were 4·8 and 0·0; the third time, 7·1 and 2·5; and on the November (the last) occasion, 4·1 and 0·0." The numbers on which the percentages are based were admittedly not large, but it is claimed for them that the indication which they furnish is too uniform to be mistaken. A newly-observed phase of school operations seemed here to have been at work; the bringing together of the school children operating again and again so as to give a serious specific quality

to throat ailments which either appeared very trivial or were altogether unrecognised; and this with remarkable and even startling suddenness. Similar experiences were soon recorded by other observers; and definite "explosions" of diphtheria have been by no means uncommonly recorded in connection with school attendances. School influence has also operated in another way, and this especially at those seasons when diphtheria is least prone to show itself in recognisable form. At such seasons the unexpected occurrence of one or more severe attacks of the disease has led to the idea that the infection might possibly be lingering amongst the school children, and under such circumstances both other observers and I myself, as the result of personal examination of the throats of pupils and pupil teachers in elementary schools, have found an unexpected and exceptional amount of throat sickness, the true nature of which has been revealed by the detection of cases of diphtheritic paralysis amongst some of those who admitted such antecedent throat or nasal symptoms as are common in mild attacks of diphtheria.

Whilst dealing with this subject I would refer to a communication I addressed to the Epidemiological Society of London in April 1878, in which, from certain of my own investigations into outbreaks of diphtheria, I drew the conclusion that under certain circumstances the property of infectiveness appeared to be a matter of progressive development, and that throat illness which under one set of conditions might remain practically non-infective, might under others become specifically infective and, in their transmission, acquire characteristics not to be distinguished from that which is clinically known as diphtheria. This view has since been accepted by a number of medical officers of health and other observers; but it has seemed insufficient to account for the explosive character of some of the outbreaks which have occurred in connection with elementary schools. On this latter point I would venture to observe that a micro-organism possessing in small degree the property of infectiveness might, under one set of conditions of throat, season, and so forth, require repeated transferences and transplantations from throat to throat before any considerable modification of its morbific qualities was brought about; whereas under other conditions of "throat culture" the stages in question might be reached at so rapid a rate as even to account for occurrences such as those met with at Pirbright.

In a former work on the subject of diphtheria I have summarised the methods in which school influence appears to be operative for mischief much as follows: — 1st, It brings together those members of the community who are, by reason of age, most susceptible to diphtheria; 2nd, The children thus brought together are placed, and remain for many hours of the day, in exceptionally close relation to each other; 3rd, The closer the aggregation and the greater the hindrance to free movement of air, the greater the risk; 4th, Faulty sanitary conditions of the schoolhouse and its surroundings, and such other conditions as tend to a condition of general ill health, in so far as they induce sore throat, favour the reception of any imported diphtheria infection; 5th, There are

ample grounds for believing that the aggregation of children in elementary schools constitutes one of the conditions under which a form of disease of particular potency for spread and for death may be manufactured; 6th, The practices of kissing and of transferring sweetmeats from mouth to mouth — practices more common among girls than boys — the joint use of drinking cups and the like must assist in the diffusion of diphtheria amongst school-fellows.

Amongst the more recent contributors to the etiology of diphtheria in connection with school influence is Mr. Shirley Murphy. He has pointed out (13) that in the metropolis there was during the ordinary late summer holiday period of 1893 a sudden drop in the number of notifications of diphtheria; and he adds "the whole of the holiday depression is due to diminished prevalence at the school-age period of life." Mr. Murphy does not regard statistics for so limited a period as conclusive; but he notes that, at least, they harmonise with other observations, and indicate the need for further inquiry into the influence of elementary schools on the prevalence of epidemic disease.

Direct Infection from Person to Person. — Incidentally this has been referred to more than once already. It is probably by far the most common cause of diphtheria, and as the fauces and respiratory tracts of the sick and healthy respectively are closely brought together, so is reception of the poison by this means the more likely to result. Young nurses who carry about in their arms little children suffering from diphtheria; relations and others who kiss persons suffering from diphtheria, whether in a recognised form or not, and children who during school attendances are packed closely together, and thus run risk of inhaling the throat or nasal emanations of school-mates having mild forms of diphtheria, — these are the sort of people who run most risk from diphtheria by direct infection.

Fomites. — The infection of diphtheria has long been supposed to attach itself both to premises and to articles of bedding, clothing and the like; and there are indications to show that in so far as premises are concerned, the faculty of the diphtheria organism for retaining its vitality is distinctly enhanced by conditions leading to dampness — especially dampness of site. Growths of ordinary mould in premises may often indicate such dampness. In a number of instances the evidence of the communication of diphtheria by means of the bedding and clothing of the sick is such that no doubt can remain of the spread of the disease in this way. Again and again the distribution of such articles amongst relations and others has been followed by diphtheria amongst their recipients, and this under circumstances of time, and of previous immunity from any throat affection, that must remove all doubt as to the relation between the two events. To name one instance only, I have known the despatch of a pillow from an infected house to another locality altogether free from any throat affections to be followed within a few days by the onset of fatal diphtheria amongst the members of the recipient family.

Milk Diphtheria. — One of the most important discoveries of modern

times in connection with the etiology of diphtheria is the relation of this disease to the consumption of milk; and it is not saying too much to assert that many occurrences of diphtheria which might otherwise have been set down to other or to altogether unknown causes, have received their explanation since the dissemination of diphtheria by the agency of milk was first demonstrated by Mr. W. H. Power in 1878 (14). Since that date many outbreaks have been traced with the greatest certainty to milk, — the disease not only having followed the distribution of a certain milk-supply again and again, even when carried to widely different and distant localities, but having been limited at the onset of the outbreaks in those special localities exclusively to persons using the milk in question.

In certain instances the infection of milk by means of the diphtheria contagium must be attributed to the exposure of milk to infection derived from antecedent diphtheria in the human subject. It is needless to discuss at any length the means by which milk can thus become infected. Wherever the throat emanations go, and whether aerially or by means of material adherent to the hands and clothes of others, there will be risk of infection; hence milk may become specifically contaminated whenever the air of the sick chamber has access to it, or where persons in attendance on the sick take part in any dairy processes. In like manner milk may become infected with the diphtheria poison when persons who are engaged either in the dairy farm or the milk shop, or who are occupied in any way in the collection and distribution of milk, are themselves suffering from diphtheria in however mild a form. And it has been shown by Dr. Klein that milk, once inoculated with the diphtheria bacillus, serves as an excellent multiplying ground for the organism even at such ordinary temperatures as 18°–20° C. (64·4°–68° F.).

But the more we learn of milk as a vehicle of diphtheria, the more probable does it become that the infection is much more frequently derived from the cow herself than from repeated specific contamination by the human subject. Thus it has happened that milk from a certain dairy, whatever the locality in which it has been distributed, has served to convey and to keep on conveying diphtheria to the retail customers; and this although all suspicion of antecedent diphtheria or "sore-throat" amongst the dairy hands could be eliminated with a degree of certainty leaving little or nothing to be desired. And this has happened when the milk, which was obviously conveying the infection, was derived from two different dairies situated at a distance from each other, and having little or nothing in common except the transference of cows from one to the other establishment. So strongly has the evidence in such cases pointed to the cow herself, that Mr. W. H. Power felt compelled to consider (as he wrote now some seventeen years ago) whether there might not have been "risk of specific fouling of milk by particular cows suffering from specific disease, whether recognised or not" (15). Later it became possible to trace the milk which conveyed diphtheria in very definite manner to certain cow-houses in which one or more cows — notably those which had recently calved — had suffered from an ail-

ment which is certainly infective from one cow to another, and is associated with certain definite symptoms, including a rise of temperature and a form of eruption on the udder and teats which, when seen in its later stages, has hitherto been commonly regarded by cow-keepers as "chapped teats." This eruption usually begins in the form of vesicles, which rapidly pass into pustules and scabs, or crusted ulcers. At a next stage in the inquiry it was found that a similar disease could be produced in the cow by inoculating the animal with sub-cultures of the diphtheria bacillus; and when this was done the material derived from the induced vesicles and pustules were in turn found to contain the same bacillus, which could be unmistakably demonstrated by cover-glass specimens and by culture. And, further, the milk of cows thus inoculated was found to contain the diphtheria bacillus in abundance.

In a number of outbreaks of that which may now without question be called "milk diphtheria," it has been found that the different incidence of the disease on individuals has come to depend, among other things, on their opportunities for consuming the milk in question. Thus well-to-do persons, largely using raw milk in their families, have suffered out of all proportion to their poorer neighbours, who could only afford a small supply, to be used in their tea. And, further, it has been found that stored milk, in the form of cream and still more so of skim-milk, has been more potent for mischief than fresh milk — the storage of milk, as, for example, when set for cream, giving opportunity for the development and multiplication in it of the contained specific organisms.

Diphtheria in the Lower Animals. — But the cow is not the only one of the lower animals which is capable of serving as a medium for the distribution of diphtheria, nor the only one to which the disease can be communicated from man. Different animals, including pigeons, turkeys, and cats, have been referred to in this connection; but, whether the matter be studied from a bacteriological or etiological point of view, it will probably be admitted that the case of one animal only is altogether free from doubt in this connection, namely, that of the cat. There are a number of instances in which human diphtheria has followed on similar disease in cats; and, on the other hand, evidence has appeared that cats have contracted diphtheria from the human subject. Dr. Bruce Low, in reporting to the Local Government Board on an epidemic of diphtheria in Enfield, expresses the opinion that a disease resembling diphtheria which he met with in the cat was in all probability first contracted from human diphtheria, then communicated from cat to cat, and then transferred again from the cat to the human subject.

Writing in 1889, Dr. Klein (16) says "that cats are really subject to an infectious disease occurring in association with human diphtheria"; and, further, that "this disease casually occurring in the cat is very similar to the malady artificially producible in that animal by inoculating it with human diphtheria." We must, therefore, recognise the fact that diphtheria in the human subject may have its origin in disease of a like sort in at least one animal common in our households, namely, the cat.

The Influence of Sanitary Circumstances. — Few questions relating to the etiology of diphtheria have led to more discussion than that which is concerned with determining the influence, if any, of faulty sanitary circumstances on the causation of this disease. The extremes of opinion are best illustrated by two classes of contentions. First, there are those who, having to deal with diphtheria, find that in the locality or house where it prevails there are certain more or less obvious faulty sanitary conditions; and these persons are content to regard the coincidence as cause and effect: secondly, there are those who, often meeting with diphtheria where there is no history of exposure to faulty sanitary conditions, have become convinced that the disease can in no way have relation to such conditions. The truth lies, I believe, somewhere between these two extremes.

In considering this question it should be remembered, in the first place, that the quarter of a century beginning about the year 1870 has been a period in which unexampled progress has been made in England and Wales in improving the sanitary circumstances under which the people are living, whether of water-supply, sewerage and drainage, the disposal of refuse and excreta, or dwelling accommodation. It has also been a period in which the general mortality from all causes in this country has diminished from the mean annual rate, for the first five years of that period, of 22 per thousand living, to one of 19 for the latest five years of that period for which we have mortality returns; in which the corresponding rate from the seven principal zymotic diseases, including diphtheria, has fallen from 4·8 to 2·5; and in which the rate of mortality from enteric fever — a disease known to be intimately associated with bad sanitary circumstances affecting water-supply, sewerage and drainage, and so forth — has fallen from 0·37 to 0·17 per thousand. But during this same period of sanitary progress, associated as it has been with a substantial diminution in the amount of death from the several causes specified, the corresponding death-rate from diphtheria in England and Wales has gone up from 0·12 to 0·19, an increase of 63 per cent; and in London and the large cities the increase has been even greater — it has, indeed, more than trebled. From these facts it would at least appear that the removal of ordinary faulty sanitary circumstances has not only not been followed by diminution in diphtheria, but that precisely the reverse has taken place. In the second place, so far as I can learn, it has hitherto been found impossible by skilled observers — including the medical inspectors of the Local Government Board, many leading medical officers of health, and distinguished foreign epidemiologists, such as Professor Fodor — to identify the use of polluted water-supplies as a cause of diphtheria. In the third place, it is certain that in the vast majority of cases diphtheria is due either to infection from an antecedent case, whether in school or elsewhere, or to infection conveyed through milk; and that consequently the balance attributable to faulty sanitary circumstances cannot be a large one. The advocates, however, of general insanitary conditions as a cause of diphtheria lay special stress on the

influence of faulty sewers and drains, and of collections of offensive refuse, garbage, and the like; it is indeed to effluvia from such sources that they are disposed to attribute diphtheria. Their contention, therefore, requires further examination.

Diphtheria, as already stated, is due to the operations of a specific bacillus, but this organism has never to my knowledge been discovered in "sewer air." Indeed, such experiments as have been made in this direction have resulted in failure. Moreover, it is contended (17) that the micro-organisms found in sewer emanations are related rather to those commonly found in the outer air — being in the main moulds and micrococci — than to the micro-organisms found in the sewage. And further when, in such outbreaks of diphtheria as I have investigated, some obvious defect leading to pollution of respired air by sewer or drain emanations was regarded as the cause of the disease, I have in almost every instance found it not only impossible to eliminate other and better established sources of infection, but also that some alternative sources of infection were generally found to have had obvious causal relation to the disease.

But after all has been said in this direction there remains a residuum of cases which cannot so easily be disposed of. These cases are, in my experience, usually limited to single attacks, to attacks in single households, or on occasion to a small group of persons having opportunity of infection from the earlier cases.

In dealing etiologically with such cases, it is impossible to ignore the fact that exposure to certain foul emanations is in certain persons often followed by sore throat; and it must be admitted that such sore throat, as also the common "household sore throat," have infective qualities, although as yet these affections have not been identified with any particular organism. Some persons are extremely intolerant of these and other morbific conditions — such as damp, cold, etc. — and when exposed to them suffer from sore throat; and it is often among such persons that diphtheria may occur almost immediately after exposure to one or other of the emanations referred to. Now a sore throat, however induced, is peculiarly favourable to the reception and subsequent local multiplication of the diphtheria organism. Children subject to chronic sore throats have often been found specially liable to contract diphtheria; and it is also matter of common observation, that convalescents from diseases, such as scarlet fever and measles — diseases in which the fauces may be denuded of their epithelial coating — are especially liable to contract diphtheria; whereas there is no corresponding liability on the part of diphtheria convalescents to contract scarlet fever or measles. In short, a morbid condition of the fauces affords a soil favourable to the lodgment and maintenance of the diphtheria contagium — the process being one of "aerial-inoculation." Another explanation of the relation between exposure to foul emanations and an attack of diphtheria is, that where diphtheria has assumed an obscure and chronic form — the local manifestations being mainly nasal or exceptionally mild — exposure to drain emanations, to cold, and damp and like conditions, has

almost certainly a tendency to induce and to accelerate the occurrence of those recrudescing attacks of diphtheria which are so fertile a source of the spread of the disease to healthy persons who associate with diphtheria convalescents.

But these explanations do not cover a number of cases in which it is, at least, certain that diphtheria prevails concurrently with opportunities for exposure to drain and other like emanations; and some observers, who do not assert that the diphtheria organism is itself conveyed by means of sewer air, contend that there are circumstances under which sore throats, which in their early stages lack specific characteristics, do definitely acquire them at a later date. When I first suggested that the theory of the "progressive development of the property of infectiveness" was necessary to the explanation of many occurrences of diphtheria, I was inclined to assume that some substantial lapse of time was an essential element in the process. But some observers, including the late Dr. David Page, medical inspector to the Local Government Board, Dr. Fosbroke, county health officer for Worcestershire, and Dr. Jacob, medical officer of health for Mid-Surrey, have recorded instances which seem to indicate that the process may begin and be completed during the stages of a single outbreak of very limited duration. Thus Dr. Jacob records "an outbreak of diphtheria which was preceded for a month by a series of ordinary sore throats," and "gradually worked up, so to speak, to the genuine characteristic form of the disease." How far the sore throats in question may, on the one hand, have been attacks of true but unrecognised diphtheria from the onset, or how far, on the other hand, such process of development as I have indicated may take place in a single individual, owing to the accelerating influence of foul emanations having special characteristics, I am unable to say; but I am bound to admit that, bacteriologically considered, we have as yet no proof that such development does occur.

In brief I would observe: — First, that the only available vital statistics as to diphtheria do not support the contention that this disease and its increase in this country are related to faulty sanitary circumstances; second, that the operation of that which is included in the term "school influence" does account to a very important extent for the increase in question; third, that much diphtheria which in former times would undoubtedly have been assigned to faulty sanitary circumstances is now found to be communicated to man through the agency of milk; fourth, that there are good reasons for believing that sore throats, which are induced by exposure to conditions such as drain emanations, render people especially susceptible to the influence of the diphtheria contagion; and, fifth, that amongst the residuum of attacks there remain a number in which there is, in appearance at least, a connection between exposure to foul emanations and diphtheria, and that some of these cases may possibly be instances in which a process of development, even in the same person, leads from a minor affection up to a major and definitely specific disease.

No attempt can properly be made to divide the causes of diphtheria into definite groups. In one sense there is but one cause of diphtheria, namely, the operations of the bacillus diphtheriæ, and the direct influence of this organism has been indicated in each of the sets of circumstances referred to. This is equally the case whether the organism be in a state of specific activity at the moment of its reception, or whether, as has been suggested, it be in a form requiring time and circumstance for development of its specific potency. The real difference between the several sets of conditions concerned in diphtheria is as follows: — Some involve conditions such as age, antecedent sore throat, dampness of soil, etc., which appear to favour the opportunities for mischief of any chance diphtheria bacilli which may be received on the fauces or other surface; the others, such as direct infection from an antecedent case, infected milk, etc., involve the reception of the infection in such form, quality, and quantity, as practically to ensure the production of diphtheria even where some of those conditions, regarded as favouring diphtheria, may be absent. Study of the operations of both sets of conditions will indicate the means of prevention.

In the **prophylaxis** or prevention of diphtheria we have to consider both the general measures which may diminish the chance of contracting the disease, and also the more immediate and active steps which should be adopted to prevent its spread when the disease is actually prevalent.

It is well to remember, and this especially as regards families who tend to suffer from "sore throat," that whilst the broad geological features of a district have not been observed to have any special influence on the development and diffusion of diphtheria, yet residence in localities exposed to cold wet winds, and on sites characterised by constantly recurring dampness of soil and retention of organic débris and other refuse, is, if possible, to be avoided. It is a matter of almost equal importance to secure the influence of sunlight and movement of air about the residences of families and persons who are regarded as exceptionally susceptible to diphtheria. These are points to be especially borne in mind in the case of old-fashioned and well-timbered country places. The adoption of general measures of sanitation, and especially the removal of those conditions of drainage, and disposal of refuse, which are believed to have some relation to the production of sore throat, should always be insisted on.

Avoidance of infection through the agency of milk can only be ensured by habitual abstention from the use of any milk that has not been previously scalded or otherwise cooked. Fortunately we know that exposure of the diphtheria bacilli to a temperature of 60° C. (140° F.) for five minutes suffices to destroy their vitality. Recent scalding, therefore, gives ample protection against diphtheria through the agency of milk, and indirectly will tend to prevent infection from other contagia, such as those of scarlet fever, enteric fever, and tuberculosis.

Ailing domestic animals, notably cats, should be avoided. The evidence of the communication of diphtheria from the latter to man does not admit of doubt.

Diphtheria being a highly infectious disease, easily communicated from person to person, and this at distances the limit of which cannot as yet be stated, the immediate isolation of the infected person should always be attempted. The most effectual form of isolation consists in the removal of the individual to an isolation hospital; but where this is not practicable the nearest available approach to isolation should be secured. Thus, the removal of a patient to the upper story of a house, when that story can be exclusively reserved for the patient and the necessary nurse and attendant, may suffice, provided strict precautions are taken to maintain the isolation. The apartment of the patient should be well ventilated; aerial communication between it and the remainder of the house may properly be hindered by the suspension, across the doorways of the infected apartments, of sheets which are kept constantly wet with some disinfecting fluid, the wetness of the sheet being an essential point to bear in mind; sputa should be destroyed by fire or by boiling; lint, rags, and the like, used in connection with discharges from the throat, nose, etc., should be burned in the apartment; all china, glass, spoons, and such articles used in connection with the patient's meals should be placed in boiling water before they are cleaned; and all communication with the remainder of the household should be avoided as far as possible. The need for stringency in these matters is often even greater during convalescence, for this is precisely the time when there is a tendency to relax them. Members of the family who are at the susceptible ages should, if practicable, be sent away from the house. On the termination of the illness all apartments and articles liable to retain infection should be dealt with (12) by such measures as lime-washing, stripping of paper, disinfection, etc. The question as to when freedom from infection in a convalescent may be regarded as complete, will be referred to in connection with the next measure.

This measure has to do with the control of school attendances. Schools of all descriptions must always be looked upon as affording exceptional facilities for the diffusion of diphtheria. Hence, in boarding-schools, for example, all forms of sore throat should be dealt with as if infective; and if, after the effectual isolation of a few first cases, the disease still shows a tendency to spread, the school should be broken up at once, and measures of cleansing and disinfection resorted to. Early bacteriological examination of material scraped from the fauces or nostrils will materially aid in a definite conclusion as to the need of such action; but even when bacteriological evidence is negative, the mere fact that "sore throat" is spreading should have great weight in forming a decision on measures of prevention. As regards the circumstances under which reassembly of scholars in boarding-schools may be allowed, useful information may be obtained from the publication of Codes of Rules by the Medical Officers of Schools Association (18). The advance

of bacteriological investigations is also certain to come to the aid of those who are concerned in arriving at a decision in this matter. In day schools, and notably in our elementary schools, early attacks of diphtheria have hitherto been apt to be overlooked; and it has not been until the attendance at schools began to diminish by reason of sickness that the matter received attention. This should not be wherever the operation of the Infectious Disease (Notification) Act is adopted. The existence of a case of diphtheria in a household should in itself be a reason why no member of that household should be allowed to attend school. If, notwithstanding the exclusion of children so circumstanced, cases of diphtheria continue to manifest themselves, and especially if first attacks in individual households are found to occur amongst children attending school, it may become necessary to close the schools for a time. The exclusion from school of scholars from infected houses or localities, or the actual closure of elementary schools, are matters in which sanitary authorities, acting under the advice of their health officers, are vested with considerable compulsory powers under the Education Code. It has already been shown that the reopening of schools after closure has often been the means of leading to a recrudescence of the disease, and to the development of a special potency in the infection. The recrudescences must now be regarded as mainly due to the fact that the bacillus diphtheriæ is retained about the fauces of convalescents for a much longer period than was formerly thought at all probable. According to experiments made in the case of diphtheria convalescents, it has been found that the specific bacillus of the disease may exist in scrapings from the fauces in a state of vitality, as shown by cultivation, for several weeks at least after all disappearance of local indications of any throat affection. Bacteriological examination of such material in each individual case is necessary where the utmost procurable certainty is desired. Where such investigation is, for one or another reason, impracticable, it may be stated that under no circumstances should a child be allowed to return to school from a household in which there has been diphtheria until at least two weeks have elapsed since the last indication of throat-mischief in any one of the family concerned.

Whenever diphtheria or sore throat of an infective type are at all prevalent in schools or elsewhere, precautions should be taken to avoid the common use of drinking-cups and other like articles; kissing among children should also be avoided.

Whilst this article is passing through the press the question of the value of anti-toxins is under investigation and discussion. It is claimed that the serum of horses which have been inoculated with diphtheria organisms, or with the chemical products of those organisms, is able, when injected into the human subject, to confer on man an immunity against diphtheria infection. As yet the use of this diphtheria anti-toxin has been almost exclusively limited to the treatment of individual cases of the disease, a matter with which this article is not concerned. But Dr. Klein has made some preliminary experiments in this country

which go to show that guinea-pigs which have been rendered immune against diphtheria, by the injection of the prepared horse serum,—inoculations which would otherwise have been fatal to them,—succumb to fresh inoculations of the same diphtheria material after the lapse of a week or two. These experiments confirm very similar ones by Behring and Roux. It is not pretended that this is the limit of immunity that can be conferred on the guinea-pig, neither has it been practicable hitherto to determine definitely to what extent such immunity, if any, can be conferred on the human subject. Protective inoculations of ordinary doses of serum seem hitherto to be effective only for about three weeks. There appear to be grounds, however, for believing that, in so far as the guinea-pig is concerned, the use of larger doses of the serum would be followed by extension of the period of protection. But for the moment the indications suggest that any such immunity is likely to be evanescent, that such utility as it possesses may be limited to the protection of individuals who have just incurred, or must run risk, of exposure to the infection of diphtheria; and that prolongation of such risk may call for repetition of the injection of the material which confers such immunity.

R. Thorne Thorne.

Bacteriology and Pathology of Diphtheria

There are but few infective diseases the bacteriology of which has been so completely worked out as in the case of diphtheria. Although Klebs, in 1883, had described a special bacillus observed by him in diphtheritic membranes, Löffler was the first who succeeded not only in separating it by growth in artificial media, but also in producing in animals by means of inoculations distinct lesions, said by him to resemble diphtheria. After its discoverers, the bacillus is generally called the Klebs-Löffler bacillus. Löffler's observations were soon confirmed by others, notably by Roux and Yersin in France, and Dr. Klein in England; but the final proof of the specificity of the B. diphtheria we owe more especially to the researches of Dr. Sidney Martin.

The Klebs-Löffler bacillus is found in every case of diphtheria; and from the results of investigations made, we may say, all over the world, we must refuse to call any lesion diphtheria, unless it is associated with that bacillus; conversely, any morbid process accompanied by this organism is diphtheria. Formerly, when physicians relied for their diagnosis merely on inspection of the affected parts, or on certain symptoms and signs, cases were excluded because they did not conform to the accepted clinical "type"; and the absence of gangrene, necrosis, or membrane was almost sufficient for a denial of the existence of diphtheria. Bacteriology has taught us that we must alter our views, and include under diphtheria many cases which, according to the older conception, would not have been called diphtheria. At the present time we frequently hear that typical bacilli have been discovered in cases which clinically

are not diphtheria: our clinical notions must then be amended and our position reconsidered. On the other hand, but a few years ago many forms of tonsillitis and laryngitis were diagnosed as diphtheria, which now by means of an adequate examination are readily excluded. We possess, then, in this organism of Klebs-Löffler, a certain test, with the help of which in competent hands it is easy to decide the true nature of a suspicious case; and the vexed discussion as to the identity or non-identity of croup and diphtheria ceases henceforth. In tubercle and in diphtheria the bacillus asserts itself with an authority which must put aside any preconceived notions.

The Diphtheria Bacillus. — This organism is extremely polymorphic, and this character greatly facilitates diagnosis. Two varieties may be conveniently described, the long and the short variety — (*a*) *Long forms:* These are perhaps to the beginner the most characteristic forms. They are generally clubbed at one or other end, and are distinctly curved or *f*-shaped, and frequently, when stained, they have a granular or segmented appearance, as they do not take up the dye uniformly. These clubbed forms are regarded by many as degeneration or involution forms; but we shall see that this idea is probably erroneous, since they are best marked in young growths. (*b*) *Short forms:* These occur, as a rule, as straight or slightly curved rods, not uniform in thickness, but generally slightly swollen at one end, or swollen in the middle with pointed ends.

It is, however, not advisable to be too strict in this division of the bacilli into types according to their size because, although we may find growths in which all the bacilli are long and clubbed, or short and straight, yet they do frequently vary in size and shape in the same culture, and on transferring a long form from tube to tube it often changes in appearance from the long to the short form, and conversely. It has also been stated that cases presenting the long forms are more virulent than those presenting the short form. This, however, is misleading and erroneous. After an extensive examination, I can say confidently that it is futile to base a prognosis on the type of organism present. Some of the worst cases that I have seen were associated with the short variety exclusively, while many less serious cases exhibited long forms only. Again, I have found colonies of the long and the short form side by side on the same agar-agar surface.

In all cases the grouping of the diphtheria bacilli is characteristic. They never form chains or threads, but are generally arranged in irregular clusters, which in structure have been aptly compared to the irregular Chinese characters which are built up of lines set unsymmetrically and at various angles. The bacilli possess no spores, and stain well with Gram's method and with ordinary aniline dyes.

Artificial Cultivation. — The media best suited for artificial cultivation are serum or serum agar-agar, glycerine agar-agar, gelatine and broth. (*a*) On the surface of gelatine the growth appears slowly, and consists at first of a series of small isolated punctiform colonies, which gradually fuse, and form a thick, opaque, uneven white or yellowish streak which is char-

acteristic and easily recognised by those familiar with the diphtheria bacillus. The middle of the streak is thick and prominent, while at the margins the growth is thinner and expands in an irregular, uneven outline. (*b*) On the surface of agar-agar or serum the separate colonies when typical are round and whitish, with a thick, yellowish brown raised centre. Lateral expansion as a rule is slow, but varies greatly; and in some cases the growth is entirely made up of minute dotlike colonies. (*c*) Growth in alkaline broth is rapid, the liquid becoming turbid within twenty-four hours at the body temperature. The reaction of the culture medium at first becomes acid, but later it is once more alkaline.

The bacilli thus artificially cultivated present the characters of type and grouping described above; they may appear either as long or short forms, clubbed, curved or straight. They do not move and they possess no flagella. It is in young cultures on serum or agar-agar especially that the peculiar clubbed and branched forms may be observed; so that we cannot regard these as degeneration forms, but with Dr. Klein may seek in them a clue to the ancestral history of the bacillus, inasmuch as they point to a mycelial origin. An attempt has been made to distinguish two types according to the size of the individual colonies on the surface of agar-agar; some diphtheria bacilli grow always in large colonies, and others grow always in small colonies. But this, again, is no distinctive character, since large colonies on subcultivation will frequently appear as small ones, and conversely; to a certain extent the smallness of the colonies seems to depend on the closeness and crowding together of the colonies.

Bacteriological Diagnosis. — Having shortly described the most leading characteristics of the Klebs-Löffler bacillus, it is well here to give as shortly a few directions as to the method to be pursued when a bacteriological examination has to be made for diagnostic purposes: — (*a*) If a piece of membrane is available, it should first be washed in several changes of sterile physiological salt solution; then a small piece is removed with a strong platinum loop, or the platinum needle is dug into the substance of the membrane. With the latter thus charged, a series of serum or serum agar-agar tubes are now streaked, three parallel streaks being made on each, passing from one tube to the other without recharging the needle, so that in the last tube the insemination is scantiest. The tubes are now incubated at 38·5° C. and examined next morning; suspicious colonies are selected, and traces thereof removed with the platinum wire, and transferred to a drop of broth on a slide. The organisms may be examined stained or unstained; but it seems to me that in an unstained condition the bacilli are more easily, and certainly more speedily recognised. (*b*) If membrane be unobtainable, the platinum loop must be passed over or pushed into the affected part, if it be accessible, and with the charged wire tubes must be inoculated in the manner already described. This is easy enough when the fauces, nose, or conjunctiva are affected, but what is to be done in laryngeal diphtheria? Experience shows that in most of these cases the bacilli may be readily

obtained from the pharyngeal or faucial — not tonsillar — secretions, and from these tubes should be prepared.

For the purpose of diagnosis a medium must be chosen which, while specially favourable to the development of the Klebs-Löffler bacillus, has a retarding influence over the organisms generally associated with the latter, such as streptococci, staphylococci, and the bacterium coli commune. From practical experience I should recommend an agar-agar prepared from ascitic, pleuritic, or hydrocele fluid containing 2 per cent of a 10 per cent solution of caustic potash, with 5 per cent glycerine and 1 per cent grape sugar. It is more easily obtained and prepared than serum or serum agar-agar, since the above exudations are always within easy reach. The selective power of this medium towards the diphtheria bacillus is truly remarkable, and its inhibitory action over other organisms quite as striking.

It must be remembered that membranes, produced by other bacteria besides the diphtheria bacilli, may appear in the throat, and that in many cases the clinical phenomena prove to be of but little assistance; a careful bacteriological examination is therefore required. In scarlatina especially membranous sore throat is common; it may be caused by pyogenetic cocci, especially streptococci, or it may be due to the Klebs-Löffler bacillus. Hench and Heubner on clinical grounds, and others guided by bacteriological investigations, state that the scarlatinal angina appearing concurrently with scarlet fever is not true diphtheria, while the membranous inflammation following some time after scarlet fever is true diphtheria. This statement, which is also supported by Dr. Klein, is only true in a general way, and must not be taken too literally; the rule is one to which there are numerous exceptions: nevertheless it is a useful rule, as it assists us materially in the early diagnosis of scarlet fever. Sore throats may appear in other infective fevers, and should always be subjected to a careful bacteriological examination; for in several cases of typhoid fever and measles, for instance, diphtheria bacilli have been found, and it has been stated that the palsy which occasionally appears in or after enteric fever is actually due to diphtheria intoxication.

As a rule, there is no difficulty for the experienced eye to recognise the diphtheria bacilli either on the surface of the nutrient medium as a colony or on the microscopic slide. Occasionally, however, there is some or even great hesitation before an opinion is hazarded. For bacilli do occur in healthy and non-diphtheritic sore throats which closely resemble the Klebs-Löffler organism, but yet are not entitled to this name. These have been named "pseudo-diphtheria bacilli." The name *pseudo-diphtheria bacillus* apparently includes several varieties and species, and must be used with caution. At present there are at least two views and over half a dozen different descriptions of the alleged pseudo-diphtheria bacillus. Some observers give this name to organisms which bear a superficial resemblance to Löffler's bacillus, but which any critical bacteriologist would not and could not confound with it; others use the term for organisms which morphologically cannot be distinguished from the typical

diphtheria bacillus, but which differ from it in so far as they fail to evince any pathogenetic properties when tested on guinea-pigs. This is not the place for the discussion of this question, but I think that we may fairly deny the claim of the former group to the title pseudo-diphtheria bacillus, just as we deny the claim of the bacillus coli communis to pose as a pseudo-typhoid bacillus. Whether, however, the virulence test is satisfactory and exclusive is a doubtful matter: on the face of it, it seems a weak reed to rest upon and, until stronger evidence is forthcoming, it is safer to regard with great suspicion any bacillus which not merely resembles the diphtheria bacillus, but agrees with it in every point except that of virulence; and this the more since Roux and Yersin have asserted that on one and the same agar-agar or serum surface we may find virulent and non-virulent forms side by side, and also since it is easy to deprive the true bacillus of its virulence. The French writers, in fact, consider that the so-called pseudo-diphtheria bacillus is a form of the true Klebs-Löffler bacillus, the virulence of which has become attenuated.

Pathogenetic Properties.— We must now briefly consider the evidence on which the specific relation between diphtheritic processes and the Klebs-Löffler bacillus has been established. (1) If we except the cat, spontaneous diphtheria is not found in animals; the diphtheria-like lesions occurring in them are due to organisms other than the Klebs-Löffler bacillus. In the cat, however, a disease characterised by broncho-pneumonia, kidney disorder, and ophthalmia is described: in the consolidated areas of the lung Dr. Klein discovered the diphtheria bacillus in considerable numbers; and on artificial inoculation local diphtheritic changes were produced. Hence Dr. Klein concludes that cats are susceptible to human diphtheria, and that in them a disease occurs, centred chiefly in the lungs, which is akin to the infection in man. Those who are acquainted with Klein's researches in this matter can hardly question the truth of his conclusions; and since we are gradually recognising that the diphtheria bacillus is capable of producing non-membranous lesions, and that, when it finds access to the lungs, it may lead to pronounced broncho-pneumonia, they gain considerably in significance. However this may be, inoculation of the conjunctiva or of the buccal mucous membrane of the cat with diphtheritic material is followed by changes closely resembling human diphtheria. Löffler, Welch, and others succeeded in producing membranous inflammation in guinea-pigs by vigorously inoculating the vaginal mucosa; and in rabbits by treating the conjunctiva or tracheal mucous membrane in a similar manner. In some instances paralysis followed the inoculation.

Subcutaneous injection of virulent diphtheria bacilli, whether of fresh broth cultures or of gelatine cultures suspended in broth, leads to death of the guinea-pigs in from eighteen to seventy-two hours. The first changes to be noticed are swelling at the seat of inoculation — due to round cell infiltration, œdema and exudation; also, as a rule, considerable local necrosis, and degenerative changes of the heart and the voluntary muscles. From the seat of inoculation diphtheria bacilli can easily be recovered,

and occasionally also from the blood and from more distant organs, as for instance the lymphatic glands, spleen and liver. The guinea-pig, being highly susceptible, is the animal generally used for these experiments: if it be inoculated in a hind extremity with a small quantity of virulent material there appears first a distinct fibrinous exudation, surrounded by more or less extensive hæmorrhagic œdema; the lymphatic glands in the neighbourhood soon swell; the exudation becomes more marked, necrotic changes take place, and the animal gradually wastes and dies, showing, besides the local lesions, hæmorrhagic redness of the suprarenal capsules, pleural exudation, and degenerative changes in the muscles and nerves. Occasionally death is delayed even in these highly susceptible animals, and then paresis or even complete paralysis of the extremities shows itself, and the nerves show advanced degeneration.

(2) The most striking morbid phenomenon in the course of human diphtheria is the loss of muscular power which accompanies or follows the acute disease. When it was shown that even these characteristic symptoms could be reproduced in the animal by artificial infection, doubt as to the specific action of the Klebs-Löffler bacillus could scarcely persist any longer. Roux and Yersin demonstrated that the inoculation of the poisonous products precipitated from broth cultures is followed by paresis, a point which has received general confirmation. Dr. S. Martin has elaborated this question still further, and has demonstrated, so far as it is possible, the chemical and physiological identity between the toxins produced in artificial growths and the toxins produced in the human body. Their inoculation into the animal is followed by the same results; namely, by paresis, primary nerve degeneration, fatty degeneration of the cardiac and skeletal muscles, and respiratory disorder. The agreement in almost all points is so close that none but those who refuse to accept the conclusions obtained through animal experiments will deny that in the Klebs-Löffler bacillus we have the specific cause of diphtheria.

(3) The last vestige of doubt must be removed by the triumphant results of treatment with antitoxin. The serum of an animal protected against the diphtheria bacillus cures diphtheria in man. As this action is specific, it follows that the animal which gave the serum was protected against an infection equivalent to diphtheria; that is, that the Klebs-Löffler bacillus is the immediate cause of diphtheria.

The Pathology of Diphtheritic Infection. — It may be said, with some degree of truth, that the diphtheria bacillus is found only in the affected area and its neighbourhood; so that the chief symptoms of the disease are due to intoxication by the poisons locally manufactured at the seat of infection. Until recently, and especially in this country, this was accepted almost as a law; recent researches, however, show that we must modify our views somewhat, for it has been demonstrated that after death the bacilli may be traced in certain viscera and organs not in direct communication with the diseased tissues. In the membranes, or at the primary seat of infection, they occur in largest numbers, and here the toxin is most copious; in distant parts the organisms, when present,

are generally scanty and the poison more diluted. Hence, with due reservations, the original statement may be allowed to stand, and we may look to the seat of infection as the source of all the trouble. At the same time, however, we must keep in mind that the bacilli may escape, and do escape oftener than is generally imagined, into the blood or more distant organs; this is true especially of those cases which end fatally, and on them most of our pathological observations are based. This question, which here can only be considered in all brevity, has been more fully discussed by myself and Mr. J. W. W. Stephens at a recent meeting of the Pathological Society. The bacilli may escape from the seat of infection along various paths: (*a*) by transference of the *contagium* to other parts of the body, as, for instance, cutaneous infections during the course of diphtheria; (*b*) by direct extension of the diphtheritic process (with or without membranes) along the open passages in communication with the seat of infection, that is, for example, from the tonsils or larynx upwards to the nose, eyes, and ear, and downwards to the trachea, bronchi, bronchioles and lung alveoli, œsophagus, stomach and intestines; (*c*) by extension along the lymphatic channels into the cervical, submaxillary, or bronchial glands; (*d*) through the circulation into the spleen, liver, kidney. Now it is evident that the first and second conditions cannot influence the generally-accepted notion of a local infection, for in the one case we have an accidental additional lesion, and in the other merely an increased area of infection by continuity; but the other two conditions, if they occur frequently, would compel us to change our views. At present we do not possess sufficient information as to how often distant glands and distant organs contain diphtheria bacilli; but from the observations of others and ourselves it is certain that in the spleen, for instance, they may be found, at any rate in fatal cases, comparatively often. Thus Frosch, Kolisko and Paltauf, Booker, Wright and Stokes, collectively discovered them there pretty often, and in twelve consecutive post-mortem examinations we obtained positive results in nine cases; hence it can no longer be doubted that an escape into the circulation does occur in lethal cases, and especially when a tracheotomy has been performed. Nevertheless for the present and in a general way we may regard diphtheria as primarily a local infection, the bacilli being found in enormous numbers at the seat of lesion, whence the deadly poison or poisons secreted or manufactured by them pass into the system.

To the pathologist, then, the toxic substances are of the utmost importance, and to them we must now turn our attention. Roux and Yersin first demonstrated that by injection of the toxic products of the diphtheria bacilli into susceptible animals the nervous lesions so characteristic of the human disease may readily be induced in such animals. This observation was followed up and confirmed by Brieger and Fränkel, and more especially by Sidney Martin in this country. Allusion has already been made to this inquiry in the general article on Infection. Youx and Yersin obtained the toxin by precipitation with alcohol and phosphate of lime, and therefore inclined to the belief that this substance

is a ferment, or, more correctly speaking, an enzyme; while Brieger and Fränkel saw in it a toxalbumin, or rather a mixture of toxalbumins. Dr. Martin's view has already been explained, but may here be once more briefly repeated, since his experiments were more thorough than those of his predecessors.

He separated from the blood, spleen and other viscera of children dead of diphtheria, albumoses (chiefly deutero-albumose) and an organic acid; the former being always present in far greater quantity than the acid. Subcutaneously injected into guinea-pigs, the albumoses produced local œdema and slight irregularity of the body temperature. When, however, they were intravenously injected into rabbits, the result was fever, or a lowering of the temperature, loss of coagulability of the blood, paralysis of the hind legs, coma and death. Oft-repeated intravenous injections of small doses were followed by fever (variable in degree), paresis (a constant effect), respiratory disturbances, loss of weight and diarrhœa. The fever may last a long time, the paresis may appear suddenly and rapidly, but its progress is slow, and the loss of weight is always tardy. The paresis is best seen in the extremities, but affects also the trunk muscles. There is no visible atrophy of the muscles and no loss of the knee-jerk. On examining the animals after death bacilli were not found, so that the lesions were due to the chemical substances; that is to say were truly intoxicative. The organic acid, like the albumoses, is a nerve poison, but not nearly so toxic. From diphtheritic membranes fibrin, hetero-albumose, traces of proto- and deutero-albumoses, and of organic acid were obtained; but the membrane extract consisted of proteid substances with minute traces of albumoses, which extracts, when administered to rabbits, produced fever, paresis and death. It is thus seen that the membranes contain proteid substances which are not albumoses, but have, nevertheless, the same action; they are, however, far more virulent than the albumoses. From pure cultures of the Klebs-Löffler bacillus the same albumoses and organic acid were obtained, and these displayed the same physiological action as the tissue substances. Dr. Martin concludes that the bacillus diphtheriæ produces the same substances in the culture media as in the tissues, that these have the same action when injected into an animal body, and that undoubtedly the bacillus of the Klebs-Löffler is the immediate cause of diphtheria. Since the membrane extract contains no albumoses worth mentioning, and yet is extremely toxic, it is possible that in them a ferment-like substance is formed which, absorbed by the tissues, splits them up by virtue of its digestive action into toxic albumoses and an organic acid; and that the albumoses thus manufactured will produce the characteristic lesions in the animal organism.

This ferment-like body or enzyme corresponds to that obtained by Roux and Yersin, and is formed in and secreted by the bacilli themselves. Martin explains the pathological process in this manner. Since the infection is primarily a local one, the organism at the primary seat of lesion secretes a potent proteolytic enzyme which enters the tissues and blood, and wherever it comes in contact with them, digests them; the

products of this digestion are toxic albumoses and the organic acid, substances which are diffusible and, on being absorbed, lead to the morbid changes and disturbances which belong to the diphtheritic infection. We have already shortly criticised this view, and we found that, tempting though it may seem, it cannot be accepted in the form in which Martin offers it (see p. 524). Besides the reasons given there, Martin has not taken into consideration that in fatal cases of diphtheria the bacilli are frequently found in the lungs, spleen, and other organs; and therefore it seems far more probable that the toxin is secreted directly by the bacilli than produced by intermediary fermentative processes. The spleen contains toxins because they have been absorbed, and often for the further reason that bacilli have found their way there; and since the bacilli are vastly more numerous in the membrane than in the spleen, we find a poison of lesser virulence in the spleen. The albumoses may be merely contaminations which happen to come down with the reagents which precipitate the true toxin; the latter is a direct cellular product of the organisms — according to Gamaleia a nucleo-albumin — which is absorbed by the tissues, blood and lymph. There is no evidence that the process of intoxication is an indirect one, the bacterial cell forming an enzyme, the enzyme producing albumoses, and the latter inducing the intoxication; on the contrary we may assume that the bacterial cell secretes its toxin, whatever its nature may be, and that the latter is absorbed as a direct tissue poison.

Whatever view we take of the nature of the poison or of the process of intoxication, the laboratory has conclusively demonstrated that the Klebs-Löffler bacillus is the cause — the specific cause of diphtheria: whether we inoculate the animal with the living germs or with the toxic products, all the characteristic symptoms and lesions of diphtheria can easily be reproduced by carefully thought out experiments.

There is, however, another point to be considered briefly, namely, "mixed infection." But rarely on examining diphtheritic membranes do we find pure growths of Löffler's bacillus; as a rule the latter is associated with various streptococci and staphylococci, many of which belong to the group of pyococci. Is their presence of significance? Foreign observers, especially Roux, Martin, and others, assert that such an association is most unfavourable, while Messrs. Washbourn, Goodall, and Card do not consider the association with streptococci on a single bacteriological examination as evidence of unfavourable import; in fact, they incline rather to the opposite conclusion. Personal observation made at St. Bartholomew's Hospital, where as a rule only serious cases are admitted, lead me to believe that the presence of streptococci in itself does not influence the prognosis; indeed that, as a matter of fact, they are rarely found absent, whether the cases be mild or serious, if a series of cultivations (two or three tubes) be made in every case. There can be no doubt, however, that secondary septic complications, such as suppurating glands, suppurative otitis media, septicæmia and pyæmia, may be produced by these organisms. Most so-called septic and hæmorrhagic forms

of diphtheria are caused by secondary pyococcal infection. It is, however, a mistake to consider all swollen and inflamed glands, and all forms of lung affections such as broncho-pneumonia or otitis media, as being exclusively caused by these pyogenetic organisms. In the cervical and bronchial glands the Klebs-Löffler bacillus is frequently found; so it is also in the lungs after death, and occasionally in the middle ear. Nevertheless it is of the utmost importance to keep in mind the possibility of a secondary infection since, when we come to treatment, we cannot expect a serum which specifically counteracts the diphtheritic process to be potent also against the pyococcal infections. For this reason the employment of an antistreptococcal serum has been suggested, and in France this plan has already been adopted. Hæmorrhagic diphtheria seems to be generally due to secondary infection, for in two or three cases examined personally, or in conjunction with Mr. J. W. W. Stephens, I found pyococci (pneumococci and streptococci) in the blood and organs; in a third case, however, the diphtheria bacillus existed in the spleen. The mortality of this kind of diphtheria is always high, in spite of the antitoxin now used; and we can readily explain the failure of the new remedy if it be a fact that most forms of hæmorrhagic diphtheria are due to secondary infection or are true septicæmia. Broncho-pneumonia has also been generally attributed to streptococci; but my own observations and those of Wright, Frosch, Stephens and others, tend to prove that in most cases we have a true diphtheritic infection in the lungs; and in almost all fatal cases, especially if the process were laryngeal, or if tracheotomy had been performed, the Klebs-Löffler bacillus can be found in the lung. This point is worthy of the fullest consideration, since it shows the necessity of active and energetic antitoxin treatment in such cases; in these the area of toxin production must be enormous, and, as the lungs are extremely vascular, absorption thence must indeed be great.

Although I feel tempted to say a few words on cutaneous and ophthalmic diphtheria, in order not to extend this article too much, I must now pass on to the morbid anatomy of diphtheritic processes.

Morbid Anatomy of Diphtheria. — (*a*) Membrane: The presence of true or false membranes was formerly considered the characteristic of diphtheria, but, as we have already seen, it is by no means essential. If, for instance, we regard the process as it occurs in the tonsils and fauces, we may have extensive membranes, or small patches or mere powdery flakes; or again we may find an entire absence of membranous exudation. There may be mere redness or œdematous swelling, or there may be a gangrenous or necrotic lesion. Yet since the membrane must, for the present at least, remain an important clinical diagnostic factor, a few lines must be devoted to its description. These membranes consist mainly of fibrin, and are either coherent patches or small whitish flocculi; they may be firmly or loosely adherent. In most cases the surface epithelium is shed in part before the deposition of fibrin begins; but membranes may also appear in, over and even under the intact epithelium. When fully formed they consist of filaments of fibrin, which form a network

enclosing within its meshes leucocytes, red corpuscles, and bacteria. The thickness and size of the fibrin filaments varies considerably and, if the membranes are firm, lamination is often seen. When detached they leave a reddened surface behind which, as for instance occasionally on the tonsils, may be in a state of ulceration; a second membrane may quickly develop on the denuded surface. Formerly distinctions were drawn between diphtheritic and croupous membranes — true and false membranes: there is, however, no reason why we should adhere to this more or less artificial division. Dr. Klein, in his report to the Local Government Board for 1891 and 1892, pp. 126, 127, summarises the more recent views tersely, and his words may be quoted with advantage: — "True diphtheritic change of mucous membrane is regarded as involving exudation into the mucosa itself — a condition resulting, under engorgement and stasis in the vessels of the mucosa, in complete necrosis of that tissue. In this latter circumstance the mucosa becomes in effect diphtheritic membrane; its superficial part contains leucocytes, its middle or main part is a reticulated fibrinous necrosed tissue, while its deeper part, that in contact with the inflamed but still living portion of the mucous membrane, contains, like this latter, leucocytes. Most text-books now represent the above anatomical conditions as differentiating croupous and diphtheritic change of mucous membrane."

So far as diphtheria is concerned, we have first, when membranes appear, a superficial exudation into the epithelial surface, with fibrin formation and degeneration of the epithelium itself. Now the necrosed epithelium gradually disappears, in part or entirely; and the underlying connective tissue or tonsillar tissue becomes covered by a fibrinous layer containing dead epithelial cells, leucocytes, and the like, which gradually extends into the deeper strata of the mucous membrane or tonsil. Fresh layers of fibrin may be added until perhaps a thick membrane is formed. In the superficial layers, which generally are the oldest, cocci may be found; while in the deeper and younger layers we often find the diphtheria bacilli unmixed with other organisms. Often enough, however, the diphtheria bacilli are found in any part of the membrane. The tissue below the membrane is in a state of inflammation, showing collections of leucocytes, or fibrinous exudation and hæmorrhages, and, according to my own observations, may be invaded by the bacilli. Healing as a rule takes place without scarring, unless the tissue defect were so serious as to lead to destruction of the mucosa. It is interesting to remark that the diphtheria bacilli, even in fatal cases, are frequently found in the leucocytes, which may be almost over-distended by the engulfed organisms. With the disappearance of the membrane the bacilli also generally disappear. In many cases, by means of careful test-tube experiments as the cases progress towards recovery, a steady diminution in the number of the specific organisms can be demonstrated. Exceptions to this rule, however, are numerous, for even after apparent recovery the bacilli may linger in the throat for weeks. In such cases they may be impaired in virulence, in others there is no attenuation. These observations show the necessity of examining

the throats of patients who have been treated in hospitals before dismissing them; such patients must not be discharged until the bacilli have completely disappeared, since otherwise they may become sources of infection.

Membranes may be seen in the mucous membrane of the soft palate and its pillars, the tonsil, fauces, and pharynx, and the larynx; and may extend also into, or appear primarily in the nose, conjunctiva, trachea, and bronchi: more rarely they extend into the œsophagus, or appear in the stomach and intestines. In cutaneous diphtheria membranes also generally cover the sores. When the process extends into the bronchi a diphtheritic broncho-pneumonia follows, as a rule; and we often observe, in the alveoli a fibrinous network enclosing the bacilli: as I have said there can be no doubt that diphtheritic broncho-pneumonia or capillary bronchitis is much commoner than is generally believed. A curious and important pathological condition is the so-called rhinitis fibrinosa, where we find membranous casts on the nasal mucosa. Clinically such cases are not diphtheria, but pathologically and bacteriologically they are so; in the cases personally examined I obtained, as others did, large numbers of virulent diphtheria bacilli. These chronic fibrinous inflammations constitute what might be called "chronic diphtheria,"—not dangerous, perhaps, to the individual, but deserving the fullest attention as a source of infection.

Besides the local changes in the parts mentioned, morbid appearances may be found, (*a*) in the lymphatic glands, (*b*) the spleen, (*c*) kidneys, (*d*) heart, and (*e*) in the nervous system. The glands, especially the cervical or bronchial according to the seat of affection, are swollen, inflamed, or even in a suppurative condition. The spleen is frequently enlarged and injected or congested, though rarely soft; the kidneys are generally pale and cloudy, and microscopically they may show evidence of epithelial necrosis, fatty degeneration, or even of actual nephritis. The muscular tissue of the heart may be in a condition of fatty degeneration, which varies to a greater or lesser degree, but is frequently absent. Of greatest interest are the nervous changes which have been more carefully studied by Déjerine, Gombault, Meyer, and Sidney Martin. The paralysis following diphtheria is due to a parenchymatous degeneration in the peripheral nerves; so that the expression "peripheral neuritis" in this connection is unjustifiable. The white substance of the medullated fibres is broken up and attenuated, or may disappear altogether; the primitive sheath remains intact, and the axis cylinders are frequently ruptured. If this be the case, the nerve fibres below the rupture undergo the Wallerian degeneration, the white substance breaking up along the whole course of the fibre, and the axis cylinder also degenerating. The different branches of the same nerve are affected to a varying degree, so that there are generally fibres intact which can still innervate the muscle if a motor nerve be affected. This explains why during life the paralysis is as a rule partial and not complete.

The sensory and motor nerves may suffer alike, and so may also the sympathetic nerves; except that in the latter case we find changes only in the axis cylinders, there being no visible medulla. Some observers

have described changes in the cells of the anterior cornu of the spinal cord, or have ascribed the nervous changes to a mild form of poliomyelitis. Martin, in the observation from which I have amply quoted, considers them all to be essentially peripheral, and has never detected lesions in the ganglia or central nervous system. This matter is still under discussion, and cannot be considered as finally settled. Meyer has described an increase of nuclei of the nerve fibres, and also nodular swellings of the nerves formed of cellular elements; but according to Martin these changes probably only indicate an attempt at repair of the nerve.

The distribution of the nerve lesions will be considered in the clinical portion of this article, and I may conclude by mentioning that, necessarily, the muscle supplied by the diseased nerves are also degenerated to a degree proportional to the nerve lesion. The muscular fibres may present advanced fatty degeneration to such an extent that all fibres are affected; or fatty fibres may be mixed with normal ones, or parts of a fibre only may be fatty. It seems that the diphtheria poisons are special nerve poisons, for Martin has shown in man that even during the course of an acute attack which lasted only five days nerve degenerations may appear.

The same observer further states that fatty degeneration of the cardiac muscle is observed chiefly in fatal cases of diphtheritic palsy or in cases which die in syncope; hence the signs of cardiac failure in diphtheria are due to a direct influence of the diphtheria toxins on the cardiac muscle: this is the more probable as the heart of the experimental animal is easily affected by these poisons.

In discussing the pathology of diphtheria I cannot conclude without saying a few words on the hæmic changes, that is, on the increase or decrease of the number of leucocytes and on the possible import of these conditions. Most writers are agreed that diphtheria is accompanied by a marked leucocytosis which increases as the disease progresses, and again diminishes during convalescence, disappearing soon after the membrane. This leucocytosis is of the ordinary febrile type, affecting chiefly the "multinuclear, neutrophile" (finely granular oxyphile) corpuscles. Gabritschewsky states that this increase in the number of leucocytes is greatest in fatal cases, and believes that a progressive leucocytosis implies a bad prognosis. After antitoxin injections the leucocytosis steadily diminishes as it does in convalescence, and the hæmocytometer is therefore, according to him, a useful means of gauging the success of treatment. Dr. Ewing does not consider the high leucocytosis to be necessarily an unfavourable sign, for it may mean merely a pronounced reaction; but he agrees with others that in fatal cases there is leucocytosis till death; in mild cases the leucocytosis is but slight, and the leucocytosis steadily decreases in favourable cases. Dr. Morse, on the other hand, does not think that the examination of the blood is of value in prognosis, because, although fatal cases generally have a well-marked leucocytosis, it is not always present, and even in the mildest

cases is often very pronounced. Judging from personal observations made at St. Bartholomew's Hospital in conjunction with Mr. E. L. Lloyd, I agree with this writer on the prognostic value of the leucocytosis in diphtheria. The daily counts made in a series of cases show that — (1) broadly speaking, a high leucocytosis signifies a good reaction, and was present in those which recovered; (2) a low leucocytosis at the height of the disease, before antitoxin has been injected, accompanies most, if not all the fatal cases; (3) the high leucocytosis of well reacting cases, after and during antitoxin treatment, steadily diminishes, the number of cells decreasing by 50 per cent in three to four days. Dr. Waldstein states that when during convalescence the leucocytosis declines, the number of "neutrophile" cells falls rapidly, while the uninuclear or lymphocytic elements increase; in the lymphocytosis he sees a prognostic sign of great value, so much so that he recommends subcutaneous injections of pilocarpin, in order to raise artificially the number and ratio of the lymphocytes.

Artificial Immunity. — Guinea-pigs, which are highly susceptible animals, can be protected against an infection with the Klebs-Löffler bacillus in various ways: (1) by means of subcutaneous injections of broth cultures sterilised by heat or attenuated by adding trichloride of iodine; (2) by means of prophylactic injections of hydrogen peroxide; (3) by a successful cure of an experimental infection; (4) by means of Behring's combined method, which consists in the administration first of attenuated cultures, followed by that of fully virulent ones or of strong toxin; (5) by means of feeding with diphtheria toxin. The serum of a highly protected animal, as mentioned elsewhere [see art. "Immunity"], when injected into a guinea-pig in a normal state, possesses the remarkable property of rendering it immune; and, when injected into one already suffering from the effects of a diphtheritic lesion, of curing it. This gives us the 6th method of artificial protection, namely, the injection of protective serum or antitoxin, and on it is founded the serum treatment of diphtheria to be discussed presently: its principle has already been fully considered [see art. "Serum Therapeutics"]. To obtain a good and active serum horses may be injected with toxins, gradually increasing in dose and virulence, or with the bacteria themselves, beginning with their dead bodies and gradually proceeding to large doses of living bacilli; or these two methods may be combined in order to obtain a serum which is both strongly antitoxic and highly protective. The immunity which this serum is capable of conferring on animals is of comparatively short duration (one to two weeks, and at most ten weeks); and when used on man is so slight as to be of little value for prophylactic purposes. Thus in a case under my own observation, a child acquired true diphtheria within two weeks after a copious administration of the antitoxin, which had been given for an angina erroneously diagnosed as diphtheria. Its curative value, however, as we shall see, cannot be questioned.

A. A. Kanthack.

Order of Development of Diphtheria

The first result of diphtheritic infection is local. The infected part inflames, and it is in and upon the inflamed surface that the morbific microbes increase and multiply. Infection of the deeper tissues and of the whole body is chiefly due to absorption of soluble venom from the place where the growth of microbes is proceeding. Thus diphtheria may be compared with syphilis: the primary pellicular inflammation of the one and the primary sore of the other being strictly analogous; from the primary lesion the secondary infection of the whole body proceeds in both cases. This close analogy was discerned by Bretonneau (5), and the most recent and complete experiments upon the lower animals have confirmed the accuracy of his opinion.

Omitting for the moment consideration of the nasal passages, the primary seat of infection is seldom any other than the fauces or the larynx. Hence two chief forms of diphtheria. The symptoms and whole appearance of the disease differ so much according to the part first affected, that many years elapsed before physicians universally accepted Bretonneau's doctrine of the essential identity of faucial diphtheria and membranous croup.[1] The question cannot now be said to exist, bacteriological researches having finally decided it in favour of Bretonneau.

Simple and Malignant Diphtheria. — From the time of Aretæus a distinction has been made between mild (or simple) and pestilential (or malignant) diphtheria. Simple diphtheria is that which is characterised chiefly by the local affection; malignant is that in which the toxæmia predominates: the blood, and through it the whole body, is poisoned by venom prepared at the primary local lesion.

A. Diphtheritic Sore Throat (Angina faucium)

In the following pages diphtheria will be described analytically, symptom by symptom, yet not without reference to the association and succession of symptoms. A general description of the disease must always be more or less imaginary, and can never tally with actual experience and matter of fact — so many are the symptoms of diphtheria, and so infinitely varied is the manner in which they are associated.[2]

[1] "You have not forgotten the celebrated *Concours*, ordered by the Emperor (Napoleon I.) at the death of the young prince, his nephew, nor the division of the great prize between Jurine of Geneva and Albers of Bremen, authors of Memoirs, in which they both declare that angina maligna is a distinct and opposite disease from croup. No matter!" (4) p. 179.

[2] "Some such descriptions, when they have conveyed the truth with great force and faithfulness, have been regarded with the same sort of pleasure with which we look upon a well-drawn picture. But, after all, they are more pleasing than profitable. Perfection in this kind was reached ages ago, yet we go on describing what has been better described before, and are venturing with rash hands still to retouch the masterpieces of Aretæus." — P. M. Latham, *Dis. of Heart*, vol. i. p. 106.

I. Prodroma. — The first symptoms of disease relate either to the fauces or to infection of the blood; the diphtheria is manifested first in the throat or not. Symptoms which are due to infection of the blood, and precede the pellicular affection of the fauces, are called prodroma or premonitory symptoms.

i. *Fever*, which is probably an early symptom in all cases, in some is the very earliest, preceding any signs of local disease. The onset is sometimes gradual and insidious, sometimes sudden and marked by chilliness, not enough to cause shivering. The temperature seldom rises above 103°. Premonitory fever is of uncertain duration, seldom lasting more than a day or two.

ii. Fever will be accompanied by its usual concomitants — drowsiness, giddiness, peevishness, aching and pains in the limbs and back; the frequency of the pulse will be increased, the digestion disordered. The digestive disorder, indicated by vomiting, disgust for food, headache, weariness and low spirits, will sometimes last fully four days before the sore throat begins, and may be (perhaps with reason) attributed to "biliousness."

iii. *Spontaneous lassitude* is, in some patients, the most marked premonitory symptom — a great sense of weakness and weariness, lasting about four-and-twenty hours before the throat becomes sore. When the lassitude exists, as it may, nearly a week before the onset of sore throat, it lies open to question whether the lassitude is to be attributed to the diphtheria or to some other form of blood poisoning (such as biliousness); whether, in other words, the specific invasion (or prodromal) period of diphtheria can last so long.

II. The Sore Throat. — In most cases the disease is first manifested in the throat or neighbouring parts, and by one or more of the following symptoms: —

i. Soreness of the throat, especially felt on swallowing, and sometimes causing cough. In young children the sore throat is indicated by disinclination to swallow. But the soreness is sometimes very slight, and may not be complained of even when examination shows that false membranes have already formed upon the fauces.

ii. Noise in breathing, snoring, breathing with mouth open, change in quality of voice — all due to swelling of fauces.

iii. Coryza, sneezing, nose-bleeding — due to simultaneous affection of nasal fossæ.

iv. Swelling of neck on one side or on both; enlargement of lymphatic glands at angles of lower jaw: pain felt in neck, especially on movement.

v. Visible appearances in the throat; these demand much more close attention: they are of four kinds, appearance before occurrence of false membrane, false membrane, swelling, and muco-purulent secretion.

1. *Inflamed Throat before Formation of False Membrane.* — When an opportunity is afforded for examining the fauces before the appearance of false membrane, they are seen to be swollen, sometimes pale and glisten-

ing, or sometimes reddish. There are no signs by which the naked eye can distinguish diphtheritic inflammation (before the appearance of false membrane) from other kinds of inflammation. Upon this inflamed surface false membrane appears sooner or later. In some cases it is formed very rapidly, for however soon the throat be examined after the first signs of local disease false membrane is seen. On the other hand several days may elapse before the angina becomes pellicular.

The diphtheritic affection of the throat does not always result in formation of false membrane, and this non-pellicular angina constitutes one form of latent diphtheria.

2. *False Membranes.* — The first appearance of false membrane is as one or several small whitish specks or patches. Although there is no part of the throat where they may not first appear, they are especially apt to begin upon the tonsil or uvula. The margins of the mouth of the tonsillar crypts are often first affected, a point which will be alluded to hereafter with reference to the diagnosis of false membranes which are diphtheritic from those which are not. The diphtheritic membrane differs much in different cases in respect of —

(*a*) Texture; being firm, tough, and coherent, or soft, loose, and friable.

(*b*) Thickness; at first, being thin, the membrane is transparent, opaline, afterwards quite opaque.

(*c*) Extent; by which the activity of the disease, so far as the throat alone is concerned, is to be judged of chiefly. But at first it cannot be said what the final extent of membrane may be; a very small pellicle may be the beginning of very extensive disease. Rapid extension is a sign of virulence: in forty-eight hours from the beginning of exudation the whole soft palate, uvula, tonsils and pharynx may be invaded, not to speak of the posterior nares, root of tongue, larynx, and even other parts, of less importance, to be named hereafter as occasional seats of diphtheritic disease.

(*d*) Adhesion to the tissues beneath, that is to say, to the mucosa; the membrane is sometimes very adherent, sometimes it can be removed by a soft brush with ease. The mucosa is left very slightly abraded and looking almost natural, or it is swollen, ragged, and bleeding. A new false membrane is formed upon the raw surface, and sometimes very rapidly, within two or three hours.

(*e*) Rapid decomposition of the false membrane sometimes occurs, and indicates a bad form of disease. The whitish colour is lost and the membrane tends to become blackish; the smell of the breath is most offensive: putrid sore throat.

These differences in the false membrane are believed to represent, to a great extent, differences in the relative abundance or activity of the several microbes growing in the exudation — whether specific bacilli, divers pyogenetic micrococci, or common putrefactive microbes. It is said that when the specific bacillus is the prevailing microbe the false membrane is tough, coherent, and not prone to decomposition;

the puriform discharge from the affected part is scanty; when the false membrane is carefully removed, the mucosa beneath seems not to be much affected and does not bleed. When streptococci are found alone, or are largely mingled with the bacilli, the exudation is softer, more pulpy, more prone to decomposition and to be attended by an abundant puriform discharge; removal of the false membrane exposes a swollen, raw and bleeding mucosa.

3. *Swelling of parts beneath false membrane* is usually proportionate to the activity of the local disease. Swelling of the fauces sometimes becomes so great in two or three days that the uvula is pushed back and invisible, even the tonsils cannot be distinguished, and the isthmus faucium is reduced to a narrow vertical slit in the middle line. In consequence of this inflammatory swelling, the soft palate may be not less than three-quarters of an inch thick, firm and tough.

4. *Mucopurulent Secretion.* — Abundant puriform discharge from the fauces occurs in severe cases so as to interfere greatly with examination. The secretion is sometimes offensive to smell. If a similar discharge (watery at first, afterwards more purulent) occur from the nostrils or ears, it may be assumed that the nasal fossæ or tympana are invaded, and the disease so much the more serious, because more extensive. The discharge from the nostril is acrid, and excoriates the upper lip in a manner quite comparable to the effect of the vesicating virus of cantharides, as Bretonneau pointed out. No doubt this diphtheritic fluid is also a powerful irritant to the mucous membranes with which it comes into contact, and thus prepares the way for the growth of false membrane. Cutaneous erysipelas sometimes starts from the point where these irritating discharges reach the surface of the body — a complication especially apt to occur in diphtheritic otorrhœa.

5. *False Membrane cast off.* — After the false membrane has ceased to grow it is soon cast off, either as coherent flakes and shreds, or soft pulpy material. The mucosa beneath is left at first somewhat reddened and perhaps swollen. Mere excessive redness soon passes away, swelling less quickly.

Ulceration of the mucosa will follow but seldom upon the false membrane being thrown off. The ulcers may be deep, and on both sides of the throat, quite like the ulcers of scarlatina anginosa; the tonsil will sometimes be destroyed so as to leave a ragged cavity; the soft palate and uvula may be extensively ulcerated or sloughy; the mucous membrane about the epiglottis and ary-epiglottic folds may suffer in like manner.

6. *Relapse.* — After the false membrane has been cast off, but before the patient has recovered from the whole disease, a renewed exudation upon the fauces may occur, and the relapse will aggravate the disease in all respects. Recurrence of diphtheria, after complete recovery from a former attack, is mentioned elsewhere.

III. Affection of Lymphatic Structures in Neck. — Swelling of the lymphatic glands at the angle of the lower jaw is usually the first sign of poisonous infection spreading beyond the fauces. This is the case even if

the glandular swelling precede the appearance of false membranes on the fauces, in which case the mucous membrane of the throat is infected by microbes, although they have not gone on to the formation of false membrane; or, as sometimes happens, false membrane may have been formed in some situation where it is not visible; for example, on the back of the soft palate. But it is seldom that lymphadenitis precedes visible pellicles on the fauces.

The degree of the glandular swelling is proportionate to the virulence of the angina faucium, but not always proportionate to the malignity of the disease; or, in other words, the most malignant form of diphtheria, which kills the patient by intense toxæmia, is not by any means always accompanied by much affection of the fauces or swelling of the neck. In bad cases swelling of the connective tissue around the glands occurs; it may be to so great an extent as to deform the whole neck from ears to collar-bones, to render the enlarged glands hardly perceptible, and even to involve the cheeks and upper part of the chest. This external swelling is sometimes tender to touch, sometimes not; it does not pit upon pressure; the skin is either pale or reddened. Erysipelatous redness of the skin over the swelling will sometimes give rise to an appearance closely resembling that of an abscess. Great swelling of the neck is sometimes associated with very great swelling of the fauces; in this case the false membrane is often thin and delicate, the disease showing itself chiefly as swelling. Much coryza, with irritant discharge, is common. The malignant swelling occurs rapidly; it may be great on the third day of disease; and death, mainly from dysphagia and dyspnœa, may ensue on the fourth day. The dyspnœa is sometimes particularly great, the frequency of respirations being nearly one hundred a minute; post-mortem the lungs are excessively inflated with air, and yet without any false membrane in the air-passages.

The external swelling is useful as a prognostic sign; if the pellicular formation be not extensive, much affection of the glands and cellular membrane of the neck indicates a virulent form of disease. It is said that the virus of bacillus diphtheriæ does not cause more than a very moderate degree of lymphatic glandular swelling, and little or no infiltration of the cellular tissue, and that the severer form of affection of the neck (cynanche cellularis) is due to the virus of micrococci.

Suppuration of the lymphatic glands, or around them, is uncommon. The more virulent forms of the disease are fatal too soon for suppuration to occur. In cases which end in recovery, if there be any suppuration, it is slow and scanty.

IV. Some rarer local lesions, that is of the mouth and salivary glands, attending diphtheritic angina faucium.

(*a*) The parotid and submaxillary salivary glands sometimes suffer in diphtheria, probably in consequence of inflammation spreading from the mouth. The submaxillary glands especially may be felt to be distinctly enlarged, and the parotid swelling, in rare cases, is sufficient to resemble the swelling of mumps.

(*b*) The mouth does not suffer severely; the tongue is furred more or less; the gums are somewhat swollen, and either pale or red, with a very thin film of fur upon them; sometimes they bleed a little, but nothing like the "scorbutic gangrene" described by Bretonneau is ever seen in England at the present day (4), (6). Small herpetic aphthæ are sometimes present, and now and then a patch of false membrane upon the lip or cheek.

The signs of diphtheria, which has spread from the throat to the nose or larynx, will be described under the heads of nasal diphtheria and diphtheritic croup. The laryngeal affection, when it supervenes upon disease beginning in the fauces, usually begins within three or four days from the onset of the angina faucium, and seldom after a week or eight days. Post-mortem, laryngeal false membranes are seldom found to be continuous with those in the pharynx. If the diphtheritic angina be of a malignant type the supervention of croup does not obviously change the aspect of the case; the patient dies just the same from debility and not from suffocation.

V. Temperature of the Body. — Diphtheria, at its onset at least, is probably always a febrile disease. The fever follows no constant type or course; as a sort of rough rule, it may be said that the fever of the onset falls on the second or third day, and that a moderate rise of temperature continues a few days longer. The temperature seldom rises above 103° or 104°, even at the beginning of the disease; when the sore throat is at its height, temperatures about 101° are more common. Diphtheria is not a very febrile disease, and the slighter forms are more febrile than the severer. Indeed, in bad cases the temperature is not only not raised, but is even depressed, temperatures between 97° and 98° being common; in the most malignant cases a temperature of 96° in the rectum has been observed.

The cause of such algidity is uncertain; it has been attributed to degenerative change in the muscular walls of the heart, but a more probable cause would seem to be the generation of a febrifuge poison; indeed, the worst cases of diphtheria and of perforative peritonitis resemble each other much in this respect of algidity.

VI. Albuminuria. — The urine, if it be often and carefully examined, will be found in very many cases to contain albumin. This albuminuria depends upon nephritis, which is in turn probably due to a soluble poison circulating in the blood.

Albumin first appears in the urine at any period of the disease before the tenth day, seldom later. Albuminuria will sometimes come on copiously, and for the first time, after the throat has seemed to have been free from disease for several days. If the patient survive albuminuria seldom lasts long, even if it have been great. In a few cases it may persist for some weeks after all other symptoms of disease have passed away. Now and then albumin seems likely to be permanently present in the urine, though whether the albuminuria is really permanent, or whether in such cases the patient's kidneys were certainly sound before

the attack of diphtheria, speaking from my own experience, I cannot be sure.

The amount of albumin affords no trustworthy prognostic sign. The urine may be highly albuminous one day, and two or three days afterwards contain the merest trace of albumin. Other things being equal, a case with albuminuria is more serious than a case without it; more patients die who have albuminuria than those who have it not, yet patients will die who have never had it, and patients will easily recover whose urine for a short time has been highly albuminous.

If the nephritis be severe the urine is scanty and very albuminous; casts and corpuscles are found by the microscope: casts hyaline, granular, and corpuscular; corpuscles having the characters for the most part of leucocytes, but some probably being renal epithelium; a few red blood disks are seen. The urine is seldom or never smoky or bloody. Complete suppression of urine is observed at the end of life in cases which prove fatal by vomiting and heart failure.

Dropsy occurs very seldom, if ever. Symptoms which can without doubt be attributed to uræmia are not met with.

VII. Hæmorrhages and Changes in the Blood. — In some cases of malignant diphtheria the affection of the blood is so profound that during life the lips and even the whole surface of the body are of a slaty gray colour, quite apart from any dyspnœa or mere respiratory lividity. The blood itself is of a dirty brown colour, which has been compared to prune juice or Spanish liquorice; but microscopical examination detects nothing amiss. Spectroscopic examinations have not been made, and the nature of the very obvious change which the blood undergoes is but ill understood.

Hæmorrhagic tendency shows itself now and then; whether dependent upon changes in the blood or blood-vessels, or both, remains unknown. Small specks or larger blotches of extravasated blood appear in the skin, mucous membranes, serous membranes and retinæ. Free bleeding from the mucous membranes occurs, especially from the nose, but also from the throat, stomach, and bowels; the bleeding may prove fatal, either very speedily or more slowly. Hæmaturia is a very uncommon event even in hæmorrhagic diphtheria. The spleen is sometimes enlarged as in purpura, and sometimes not. Hæmorrhage, even when too scanty to be the cause of death, will do much towards increasing the weakness of the patient; such cases are always to be deemed serious.

The hæmorrhagic tendency bears no proportion to the affection of the throat; indeed, the latter may be so slight that the diphtheritic character of the disease shall be wholly overlooked, and the death of the patient be certified as due to purpura hæmorrhagica.

Cerebral hæmorrhage of the same nature is a cause, but a very uncommon cause of hemiplegia.

VIII. Failure of Heart. — In diphtheria the function of the heart is more apt to fail than in any other virulent disease which we meet with in our country. This primary debility of the heart (vital debility,

lipothymia), not due to exhaustion of the powers of the whole body, but to a peculiar operation of morbid poison upon the heart itself, which is selected as it were for this effect, constitutes the primary or protopathic malignity of the older writers (Stoll, for example) — the word malignity being used in a much more restricted sense than that referred to on page 731. The cause of the heart failure is degeneration of its muscular walls (myocarditis); when degeneration is not found after death (if this ever be the case) the heart failure must be attributed to paralysis of the cardiac branches of the par vagum.

A sign of this affection of the heart is found in the pulse, which becomes small and weak; it is often irregular also, in some cases it is very frequent, in others very infrequent. The temperature of the body falls even as low as 95·5° in the rectum; the skin and limbs are cold. The first sound of the heart is weak or quite inaudible, sometimes a systolic murmur at apex or base springs up. Unpleasant fluttering or palpitation of the heart may be complained of, and the weakened pulmonary circulation may be indicated by shortness of breath. The face becomes remarkably pale. The patient is sensible of great muscular weakness, is very sluggish, dislikes to be moved, and even takes food unwillingly.

These symptoms often come on gradually, the patient's heart steadily becoming weaker and weaker; patients of this kind may lie a week or ten days in a state of prostration. But the symptoms sometimes set in suddenly, all at once faintness (lipothymia, collapse) occurs, attended by a marked change (which cannot be described) in the look of the patient's face, and by the aforesaid signs of heart failure. The patient may die suddenly and unexpectedly, but usually he lingers for some hours in a state of extreme prostration, consciousness is retained to the end, and the power of the voluntary movements is in remarkable contrast with the weakness of the heart muscle.

Failure of the heart is usually met with during the height of the diphtheritic disease, say at any time between the fourth and fourteenth day. A slight affection of the throat may be followed by serious disorder of the heart. When the heart fails later it is especially associated with paralytic symptoms.[1]

Signs of dilatation of the heart and a systolic murmur sometimes occur during convalescence, and may be expected to disappear when the health of the patient is fully restored. If endocarditis and pericarditis ever occur as a result of diphtheria they are probably dependent upon micrococci.

IX. Vomiting. — Another serious symptom, and one often associated with cardiac failure, is a tendency to vomit. The cause of it is not always the same. But whatever it be, repeated vomiting is a dangerous

[1] Rabot and Philippe (7) describe an interstitial myocarditis which occurs during convalescence from diphtheria, when the patient has been allowed to get up, and thinks himself to be well. This form of disease must be uncommon. [I remember such a case in the private practice of the late Dr. Fuller. The patient, a young man, convalescent at the seaside, rose quickly from a sofa and fell back dead. The autopsy revealed "degenerated heart." — Ed.]

symptom; most of such patients die in a state of heart failure and algidity within a few hours or a few days.

In very rare cases vomiting is a sign of diphtheria of the stomach.

In most cases vomiting is associated with affection of the kidneys. Sometimes the urine is highly albuminous and scanty, or even completely suppressed; the diminished secretion is probably in greater part dependent upon the vomiting. Sometimes the quantity of albumin in the urine is small; sometimes the renal affection is manifested more by corpuscles and casts in the urine than by much albumin. The patient retains consciousness. Convulsions in rare cases precede death.

Now and then vomiting occurs late in the disease, in the course of paralysis, four or five weeks from the onset of the diphtheria.

X. Paralysis. — The period at which paralysis occurs in the course of diphtheria is uncertain, and very variable. Palsy sometimes sets in while the primary disease (the formation of false membrane) is progressing, say as early as the fourth day. On the other hand, as much time as ten weeks may intervene between the onset of the diphtheria and of the palsy. The mean interval, computed from many cases, is three or four weeks. More often than not paralysis may be called a sequel of diphtheria; that is to say, a period of convalescence intervenes between the primary disease and the paralysis.

Palsy may be consequent upon any form of diphtheria, yet diphtheria which is mainly or altogether laryngeal is seldom followed by palsy; indeed, few patients survive the primitive disease. The patellar tendon reflex is lost in some cases of diphtheritic croup, and this symptom may be regarded as akin to palsy. Some of the cases in which the tube cannot be removed after tracheotomy are probably of the nature of laryngeal palsy. Anything like extensive paralysis after diphtheritic croup must be most uncommon.

Diphtheria of the fauces is by far the commonest primitive lesion, indeed, there is seldom any other. About one-tenth of all cases of diphtheritic sore throat are attended by paralysis sooner or later. It mostly begins after the second week of the angina; it may occur much sooner, as mentioned above; seldom later than the seventh week. (Paralysis after nasal diphtheria is referred to further on.)

The usual course of the palsy is this, that it gradually increases until the patient dies, or until the disease begins to decline as gradually as it arose. In the latter case recovery is complete.

There is no proportion between the severity of the primary disease and of the palsy; or at least paralysis often ensues when the primitive diphtheria has been very slight. Indeed, in some cases the sore throat altogether escapes observation, the paralysis being the first evidence of diphtheria.

The fauces, and especially the soft palate, usually suffer first. The signs of palsy of the soft palate are two: the voice becomes nasal, and drinks are apt to return through the nose; moreover, the patient can hardly blow out a candle, inflate the cheeks, suck or gargle. The palate

will be seen to have lost its arching, and to hang straighter than natural on both sides. The sensibility of the mucous membrane and the reflex movements are more or less diminished. These signs are sometimes more marked on the one side of the palate than on the other; or they may even be present on one side alone. Palsy, insensibility and abolished reflex by no means always concur: one or more of these symptoms may be absent; for instance, the reflex may be lost though sensibility is retained. Paralysis of the lowest constrictor of the pharynx is indicated by entry of food into the glottis, causing choking and cough.

Paralysis is often confined to the fauces and spreads no farther; in this case it will last ten days or a fortnight and then begin gradually to disappear. The fauces sometimes escape even though the limbs and trunk are severely affected. Sometimes paralysis diminishes in the fauces as it increases in the limbs.

Paralysis of the rima glottidis is indicated by weakened voice and inefficient cough, both dependent upon imperfect closure of the glottis. Together with the paralysis go insensibility and deficient reflex of the epiglottis and interior of the larynx. Hence great danger of pneumonia from entry of food into the windpipe; great danger of suffocating bronchitis also, from deficient expectoration. Recovery from laryngeal palsy is possible.

Paralysis of the limbs affects the legs before the arms; indeed the arms often escape. When the patient is able to walk at all the gait is staggering: at last he becomes unable to stand, or even to move the legs in bed. Palsy of the limbs usually takes about seven weeks to reach its height. The muscles tend to waste, and sometimes waste greatly; partly in consequence of the nerve disease, but partly in some cases from insufficient feeding. The electrical reactions of the nerve-trunks are normal. The excitability of the muscles to faradisation is diminished or even wholly lost; voluntary power is sometimes much lessened while faradic excitability remains normal; in some instances faradic excitability will go on diminishing, while voluntary power is increasing. The degree of galvanic excitability of the muscles is uncertain; it is often diminished or slow, may possibly be increased for a time, and sometimes, not always, there are qualitative polar changes. Abnormal electrical reactions can sometimes be discovered long after voluntary power over the muscles has been completely restored. Sensibility is mostly retained; when lost it is seldom lost higher up than the knees. Patellar reflex is abolished as a rule, but is sometimes retained even when the palsy is great. On the other hand, patellar reflex is sometimes lost for a considerable time during or after diphtheria, although the legs never show any weakness. When the reflex returns it has been noted, in a few rare cases, to be excessive for a time, and to be associated with ankle clonus. The palsied limbs are sometimes painful. Recovery of the proper use of the limbs, and of normal electrical reactions, will certainly occur, and is only a matter of time. But the time necessary is often considerable, and may amount to six or eight months or more.

The hemiplegia which occurs now and then in the course of diphtheria is a different form of disease, being due either to cerebral hæmorrhage or to embolism of the cerebral arteries; in the latter case the source of the embolus is not always discovered. [*Vide* section on Cerebral Disease.]

The muscles of the trunk sometimes suffer in the ordinary form of diphtheritic paralysis, but the case is not rendered more serious thereby unless the diaphragm and intercostals be paralysed. A cause of death is paralysis of the respiratory muscles. The sphincters are very seldom affected.

The eyes sometimes suffer. The commonest affection is dimness of sight, due either to asthenopia consequent upon paralysis of the ciliary muscle (cycloplegia), or to amblyopia consequent upon retinal insensibility and contraction of the field of vision; in the latter case glasses are useless. Any form of ophthalmoplegia externa, indicated by diplopia or squint, is less common. Incomplete blepharoptosis has been observed. The pupil is unaffected, or at most but somewhat dilated and sluggish.

Palsy of the œsophagus, tongue, lips, cheeks, are possible but very improbable occurrences. The failure of the heart is in some cases perhaps of a neuro-paralytic nature.

In children and in some epidemics death is not seldom the end of diphtheritic palsy. When death does not ensue complete recovery is certain sooner or later. The duration of paralysis in cases of recovery depends much upon the extent of the affection. When confined to the soft palate recovery may be expected in two or three weeks; when the limbs are affected the duration will probably be three or four months. A duration of eight months, or even more, has been noticed in rare cases. Excluding cases of heart failure death is due either to laryngeal or respiratory palsy. Laryngeal palsy causes death through inability to cough and to expectorate properly, the result being accumulation of mucus in the lungs. Death is seldom due to impaction of a morsel of food in the larynx. Pneumonia from the entry of smaller particles of food into the windpipe is a much more common event, especially in cases of tracheotomy, or of anæsthesia of the glottis.

When paralysis follows nasal diphtheria, the fauces may be unaffected while the limbs suffer severely.

Although good observers have found changes in the medulla oblongata and spinalis in cases of diphtheritic palsy, yet the prevailing opinion is that the chief and often the only cause of the paralysis is multiple neuritis. The cause of the neuritis is supposed to be a specific soluble poison; the palatal palsy which follows palatal diphtheria looks like a purely local effect of the poison.

XI. Eruptions. — Besides the purpura and erysipelas which have been already referred to, erythema and urticaria of no constant or peculiar characters have been observed. Suffusion of the skin, almost scarlatiniform, is common.

XII. Arthritis. — Rheumatoid affection of the joints has been observed in rare cases and in some epidemics.

Diagnosis of Diphtheritic Sore Throat. — Diphtheritic sore throat is not in all cases attended by the formation of false membrane, and is therefore sometimes indistinguishable by the naked eye from simple or catarrhal sore throat. The proof of this assertion is afforded by two facts: First, that the bacillus has been found to exist upon the mucous membrane of throats which were, to the naked eye, simply slightly reddened and swollen. Next, observations made in epidemics of diphtheria have rendered it certain that the disease is sometimes transmitted by cases which have the characters of simple catarrhal or inflamed sore throat. (See Latent Diphtheria.)

But the diagnosis of diphtheritic sore throat relates mainly to the false membrane. Inasmuch as not all sore throats accompanied by false membranes are diphtheritic, we endeavour to distinguish the different kinds of pellicular angina faucium. Even if it were admitted that the bacillus is the absolutely peculiar and necessary note of diphtheria, yet it is clear that for the immediate needs of practice a mere inspection of the throat must be relied upon, and it is in this spirit that the following remarks upon diagnosis are written: —

1. Many vesicants and escharotics, when applied to the fauces, produce appearances which closely resemble diphtheria. Cantharides, lunar caustic, nitric acid, liq. ammoniæ, carbolic acid, white precipitate, hot chestnuts or potatoes, boiling water and steam, may be mentioned as instances of such irritants. The diagnosis in many cases cannot be made from the look of the throat alone. The conditions which led to the pellicular inflammation must be known.

2. The disease (or rather the diseases), which in England is most commonly called follicular tonsillitis, demands very careful consideration in regard to its relation with diphtheria. Many cases of this follicular tonsillitis are diphtheria in an early stage, the appearance of ulceration round the mouths of the tonsillar crypts being due to false membrane, which often is first formed in that situation. The membrane may spread afterwards so as to cover the greater part of the fauces in two or three days. In other cases the membrane does not spread upon the fauces, but laryngeal diphtheria is associated with the tonsillar affection; in others again the membrane does not spread in any direction, and the true nature of the disease becomes apparent only when the patient infects another person with manifest diphtheria: or the reverse may be the case, that the disease conveyed from a person suffering from manifest diphtheria will take on the form of follicular tonsillitis in the infected patient. But although in all these cases there can be no doubt concerning the diphtheritic nature of the follicular tonsillitis, yet it seems to be equally certain that in other cases the disease is not diphtheritic, those, namely, which show no contagious tendency. But admitting this distinction, it can seldom be drawn in a given patient, and therefore in practice it is wise to consider the disease to be in all cases probably, or at least possibly, diphtheritic.

3. Herpes, of the same nature as herpes labialis, may affect the palate

so as to produce the appearance of one or more small false membranes which show no tendency to spread after they have once been formed. The diagnosis (not always certain) is much helped by the concurrence of herpes on the tongue, cheeks, or lips.

4. A fungus (oidium albicans ?) sometimes affects the fauces, and causes them to be covered by a growth which looks like a false membrane, and which may be so extensive as to cover the soft palate and tonsils. Compared with the false membrane of diphtheria, the growth of oidium is of a purer and more opaque white colour, it is much softer also, and when once it has been removed by detergents it seldom reappears. Microscopic examination is easy and decisive.

5. A fungous growth (leptothrix buccalis ?) sometimes occurs within the crypts of the tonsils, and, coming to the surface, simulates follicular tonsillitis. Or the growth may spread over the tonsil so as to form a white patch. The chief distinction from oidium and pellicular diseases is to be found in the fact that the leptothrix affection is essentially chronic.

6. At any time during the first week of scarlet fever false membrane may appear upon the fauces. This membrane is said to be due to micrococci, and not to afford the Klebs bacillus. Yet by the unaided eye the exudation, which is sometimes abundant, is not to be distinguished from that of diphtheria. The diagnosis depends mainly upon the eruption. The scarlatinal false membrane is very much more prone to be followed by ulceration than is the diphtheritic, and the lymphatic glands are much more likely to suppurate. It is quite true that scarlet fever does not often affect the larynx, yet in rare cases of that disease false membrane may be found even there. Subsequent paralysis does not occur. True diphtheria may complicate scarlet fever during the second or third week, and may occur in scarlatinal nephritis at any stage.

7. The mucous tubercles of syphilis, when they involve the fauces and before ulceration sets in, may resemble diphtheria closely.

8. In rare cases of typhoid fever and early in the disease, false membrane forms upon the fauces; it does not last for more than a few days, but it cannot be distinguished from diphtheria until the course of the disease is manifest.

It seems unnecessary to do more than refer to the faucial affections of small-pox, chicken-pox, and pemphix. The ulceration of tubercular angina faucium is sometimes at first mistaken for diphtheria. And the same is true of that very uncommon disease, primary gangrene of the fauces.

Recurrent Pellicular Angina. — Some forms of pellicular angina are very prone to recur, and the recurrences may be frequent, for example, once every two or three months for a year or two, or even as many as four attacks in twelve weeks. The appearance of the throat is that of slight diphtheria (or follicular tonsillitis); but the precise nature of the disease is doubtful, and it is equally doubtful whether that nature be the same in all cases. This recurrent pellicular angina is often a very febrile disorder, is not attended by albuminuria, nor followed by paralysis. It can seldom be traced to insanitary conditions; and when it recurs fre-

quently it seems to be probable that the contagium vivum lurks about the throat in an inactive state. In many cases the disease is but slightly if at all contagious.

An attack of true diphtheritic sore throat does not protect against recurrence of the disease. Yet as a rule (which, however, does not always hold good) recurrent diphtheria is not so severe and dangerous as the first attack.

Prognosis. — The prognostics which may be derived from individual symptoms will be found scattered through the preceding pages and need not be repeated here.

The cause of death differs in different cases. (i.) Suffocation by extension of disease to the larynx is common. (ii.) Poisoning of the blood (malignant diphtheria) is a less common cause of death. This malignity is indicated by nasal discharge, glandular swelling, erysipelatous redness of the skin over the swelling, tendency to hæmorrhage, failure of the circulation (as shown by a bad pulse, pallor, and coldness of the surface), and delirium. Death is often sudden. (iii.) Heart failure. (iv.) Palsy of respiratory muscles.

Recovery of the former state of health is sometimes a very slow proceeding, even excepting the cases of paralysis.

Treatment.[1] — From the remotest ages of medicine it has always been assumed that the foremost indication for the treatment of diphtheria consists in disinfection of the primary disease, which is usually that of the throat. Both laboratory experiments and clinical experience point to carbolic acid as the germicide which most of all combines efficacy and safety. It may be used in a solution as strong as twenty per cent in the case of children, and thirty per cent in the case of adults. Glycerine, castor oil, and rectified spirit have been much employed as solvents for the acid; sulphoricinic acid has of late been recommended as the vehicle (8), under the belief that it affords the least painful application; I have used this sulphoricinic phenol and believe it to be efficient for the purpose. Remove as much of the false membrane as possible by means of some close soft material ("molleton" is suitable) (9) tied on the end of a probe or an osier twig, or held by forceps, and afterwards apply the carbolic solution freely to the denuded surface. Should the false membrane continue to form and to show signs of spreading, the treatment may be repeated once or oftener, according to the discretion of the physician. These applications to the throat tend to exhaust the strength of the patient, and the doctrine of local disinfection may be carried out in practice to a dangerous length. The frequent use (for two or three minutes every hour) of a spray of a saturated solution of boric acid is always serviceable, whether the throat be also swabbed with carbolic acid or not. If deglutition be painful it is well for the patient to benumb his fauces by means of ice before attempting to swallow.

The most important part of general treatment consists in feeding the

[1] For the serum treatment refer to the last chapter.

patient, and milk is the most suitable article of food. It should be given every two hours by day, and every three hours by night. Brandy is useful and even necessary in many cases, especially if an insufficient quantity of milk be taken, or if the patient be exhausted, or if the heart show signs of failing. Should the patient refuse to take the necessary quantity of food he must be fed by means of a soft catheter passed through the nostril into the œsophagus.

It is not possible to lay down any universal rule concerning the employment of drugs. None are specific, and the indications for their use must be left to the judgment of the practitioner who is directing the treatment of a case. Chlorate of potash is cleansing to the mouth, but to give the salt in large doses is useless or even dangerous. The old-fashioned chlorine mixture[1] is the best way of giving the chlorate.

Signs of heart failure should be carefully watched for. If they appear the patient must be kept as still as possible in the recumbent position, and he must not be allowed to sit up, still less to get out of bed, for any purpose. Alcohol and strychnia are the best medicines.

If there be any signs of laryngeal paralysis the patient must be fed by means of a tube through the nose, and by nutritious enemata. The use of the tube is favoured in most cases by insensibility of the fauces and pharynx. If vomiting follow the first use of the tube the practice should not therefore be given up, for the vomiting is seldom repeated. The patient must be watched, and if he vomit he must be turned over on his side, with his head low, so that the vomit may not enter the larynx.

Treatment of palsy of the limbs is guided by the knowledge that, if the breathing muscles escape and the heart do not fail, the patient will recover. The chief means of promoting recovery consist in rest and in maintaining or improving the nutrition of the whole body. Massage and electricity may be used, but must be used gently. In respiratory palsy faradisation of the phrenic nerve has been known to do good.

For the vomiting and the purpuric state no treatment avails; the nephritis must be managed upon general principles.

B. Diphtheritic Croup (Laryngitis)

That is to say, diphtheria which causes predominant laryngeal symptoms, is discovered by means of the laryngoscope, or of the expectoration, or of certain indirect signs of the disease.

I. Laryngoscope. — The use of the laryngoscope, which is not always easy even in the case of adults, is difficult or quite impossible in the case

[1] Put ten grains of powdered chlorate of potash into a pint bottle, and add half a drachm of strong hydrochloric acid. Keep the bottle corked until the effervescence has ceased; then add an ounce of cold water and shake the bottle well, not allowing the gas to escape; then add another ounce of water, and again agitate well, and so on until the bottle is full. The resulting solution does not taste nearly so badly as it smells; a little sugar may be added. A tablespoonful or two, according to the age of the patient, may be given frequently. An adult may take the whole pint in the day. Chlorine vapour was recommended by J. Johnstone as early as 1779.

of children, especially young children. Hence it seldom avails much in the diagnosis of croup;[1] however, in a case of doubtful nature it is always well to try what the laryngoscope can show. A small, warmed mirror can be passed back into the fauces without any attempt to depress the tongue or to draw it out of the mouth, and in this way the epiglottis, at least, can be seen, if there be not much gurgling of frothy mucus in the throat. Should false membrane appear this is enough, but it need not be said that the nonappearance of membrane proves nothing.

II. Expectoration. — Children seldom expectorate false membrane before tracheotomy has been performed; ejection of false membrane through the tracheotomy wound is a very common event. Yet even after tracheotomy for diphtheritic croup it may happen that no false membrane will at any time be seen. Adults, on the other hand, suffering from diphtheria strictly confined to the windpipe, will sometimes expectorate false membrane in large quantities, and this even when the dyspnœa is slight and the chief laryngeal symptom is dysphonia.

III. Signs of Laryngeal Disease. — In most cases the diagnosis depends upon certain signs which indicate derangement of the laryngeal functions. These functions are two — vocal and respiratory: vocal, that is the proper and peculiar function of the larynx, the larynx being the organ of voice; respiratory, that is transmission of the breath, the larynx being part of the windpipe. The signs of disease correspond with these functions. Disorder of the vocal function is indicated by dysphonia; disorder of the respiratory function, by laryngeal dyspnœa and laryngeal stridor. To these must be added a third sign, wholly adventitious, allied to voice on the one hand and to breathing on the other, namely, a peculiar stridulous or laryngeal cough.

1. *Dysphonia.* — As the voice is the peculiar function of the larynx, so dysphonia is the pathognomonic sign of laryngeal disease. Dysphonia relates to the quality or to the loudness of voice. (*a*) When the quality of the voice is changed it is called paraphonia, of which hoarseness is the commonest form, being a lesion of the simple glottic sound and not of the articulated voice. (*b*) When the loudness of the voice is diminished it is called aphonia, a term which implies not only absolute privation of voice, but also any degree in diminution thereof. When aphonia is complete the patient can speak only in a whisper — whispering being articulation pure and simple without any glottic sound.

2. There is nothing pathognomonic about the disordered respiratory functions met with in laryngeal disease. Laryngeal stridor and dyspnœa have to be distinguished from other forms of stridor and dyspnœa; and this can be done by determining the presence or absence of certain by-symptoms (*signa assidentia*). (*a*) By stridor is meant a sound which is produced in the windpipe (larynx, trachea, bronchi) by breathing, and which can be heard without auscultation. Stertor, on the other hand, is a sound which breathing produces in the parts above the windpipe.

[1] For exact definition of the word Croup, see *Medico-Chir. Trans. for* 1879, vol. lxxii. p. 27.

Narrowing of the windpipe is the cause of stridor, and its loudness depends upon the swiftness of the air-currents; hence when the narrowing of the air passages becomes great, and the air currents become correspondingly weak, stridor diminishes or even disappears. The peculiar quality of stridulous breathing is a fact which must be taught by experience, and which cannot be described by words. (*b*) The characters and associated symptoms of laryngeal dyspnœa are these: — (*α*) The dyspnœa is chiefly inspiratory or expiratory; usually the inspiratory movement is much prolonged, but it may happen that the expiration will be at least twice as long as inspiration. (*β*) The dyspnœa affects the movements of both sides of the chest, inspiratory dyspnœa being marked by powerful contraction of all the inspiratory muscles, and by recession of the yielding parts of the chest, expiratory dyspnœa being marked by powerful and prolonged contraction of all the expiratory muscles. (*γ*) The breath-sounds heard by auscultation are weakened. (*δ*) The nostrils dilate during inspiration or expiration, or are permanently dilated. (*ε*) The up and down movements of the larynx (depressed during inspiration) which attend respiration are much increased in laryngeal dyspnœa; similar movements of the lower jaw are sometimes to be seen. (*ζ*) The radial pulse is withdrawn from the finger during inspiration in severe laryngeal dyspnœa.

3. The stridulous cough (or croupy cough), a most important sign of laryngeal disease, does not admit of being described in words.

IV. Course of Disease. — In a case of diphtheritic croup dysphonia and stridor mostly precede dyspnœa, inasmuch as dyspnœa requires a greater amount of disease than suffices for the production of dysphonia and stridor. The voice is more or less weakened (aphonia) and husky (paraphonia), yet in strict truthfulness it must be said that sometimes the voice is very little affected, or even not at all. The breathing, instead of being silent, becomes dry and husky, characters more marked in inspiration than in expiration. The cough is usually dry and husky; sometimes it is loose; and sometimes there is a loud barking cough (*tussis ferina*); the noisier the cough the less the obstruction.

Dyspnœa follows, often the day afterwards; but, as a rule, it does not attain a high degree for another day, or even for two or more days after its onset. There are no remissions, worthy so to be called, in the dyspnœa; when once it sets in it abides, except that it sometimes abates shortly before death. Moderate dyspnœa may at any time become suddenly very great so as to demand instant tracheotomy.[1] In adults the dyspnœa comes on later, progresses less rapidly, and is less severe than is the case with children — the reason of the difference being due chiefly to the relatively small size of the glottis in children, but partly to the more powerful inspiration of the adult, and to his smaller liability to collapse of lung.

[1] Should the reader require a picturesque description (in the style of Aretæus) of the dyspnœa of croup, he may refer to Trousseau, who has performed this work once for all (Trousseau, *Clin. Méd.*, New Sydenham Soc. vol. ii. p. 477).

V. Comitant Symptoms. — 1. The *lividity* of the patient is not exactly proportionate to the dyspnœa. Sometimes there is but little lividity, or even none at all, though the dyspnœa be permanent and at intervals great. Lividity is often due in part to associated pulmonary disease, bronchitis (catarrhal or diphtheritic), congestion of lungs, or collapse.

2. The *fever* is not high. Indeed, the temperature is often normal, or even subnormal, especially when the lividity is great. When the lividity is not great the temperature may rise to 102°, or if the fauces be affected, even higher. Scarcely need it be said that tracheotomy interferes with the course of temperature.

3. The *fauces* often look healthy, but even upon apparently healthy fauces specific bacilli may breed. In some cases small or extensive false membranes will be seen.

4. Puffiness on one or both sides of the *neck* may exist, or even an enlarged gland or two, the fauces being natural.

5. *Albuminuria* is common, yet sometimes there is none even in fatal cases. There is often an excess of flocculent deposit containing leucocytes.

6. Symptoms of the virulent kind, due to poisoning of the blood, do not occur. Paralysis (except, perhaps, glottic paralysis) does not follow diphtheritic laryngitis, yet the patellar tendon reflex will sometimes be lost for a long time after an attack of membranous croup in persons who were known to have such a reflex before they suffered from diphtheria.

Prognosis. — 1. Recovery occurs in a very small proportion of the cases of laryngitis which have been proved to be diphtheritic by the expectoration of false membrane, or by the comitant affection of the fauces.[1] Tracheotomy saves a few lives, but recovery may occur without tracheotomy. The younger the patient the smaller the chances of life, for reasons which have been already referred to when speaking of dyspnœa; but even children of less than a year old may escape with life, after having expectorated false membrane.

The feeble and husky voice and croupy cough will remain for a week or more after the dyspnœa has ceased, both in cases which have undergone tracheotomy and those which have not. The laryngoscope, when it can be used, does not always afford an explanation of these symptoms.

Recovery after tracheotomy is sometimes imperfect, that is to say, the tube cannot be removed; the reasons of this will be given hereafter.

Relapse occurs in rare cases; the patient has survived the worst period of the disease, and seems to be convalescent, although not quite well, when the diphtheria breaks out again in full vigour, and will probably kill the weakened patient.

Diphtheritic croup very seldom recurs after an interval of perfect health. But it is a disease which does not often give the patient a

[1] The serum treatment enables us to give a very much more favourable prognosis in cases of laryngeal diphtheria: see the last chapter.

chance of undergoing it a second time. The croup which recurs is of the catarrhal and spasmodic kind.

2. Death is due to one of two causes, either to laryngeal or to pulmonary dyspnœa.

(α) Laryngeal dyspnœa is a cause of death which is now usually prevented by tracheotomy. The duration of cases which are fatal without tracheotomy is two, three, or four days from the onset of the croupy symptoms. Unfavourable conditions which aggravate the fatal tendency of croup are infancy and rickets, for reasons which are sufficiently obvious.

(β) Pulmonary dyspnœa is due to many causes: — (i.) Extension of the inflammation downwards into the lungs, the smaller air-tubes becoming choked by false membrane, or more commonly by creamy muco-pus; upon this condition lobular pneumonia (catarrhal or broncho-pneumonia) is very apt to supervene. (ii.) Congestion of the lungs, which occurs when the lungs cannot inspire more than from one-fourth to one-half of their normal supply of air. (iii.) Collapse of lungs more or less extensive. (iv.) Acute emphysema (or insufflation) of the front part of the lungs beneath the sternum and the neighbouring cartilages. (v.) Inability to cough and consequent retention of secretions. (vi.) Pneumothorax, which is not uncommon in fatal cases which have undergone tracheotomy.

Pulmonary dyspnœa mostly sets in from four to seven days from the onset of the croup. Hence it is especially seen in cases of tracheotomy, because other cases of laryngeal diphtheria by the end of the first week are either dead or recovering. The dyspnœa sometimes becomes very great all at once.

The signs of pulmonary affection are these: — (i.) Increase of fever, especially in bronchitis and pneumonia. (ii.) Physical signs of bronchitis, extensive collapse, insufflation of lungs, or pneumothorax. (iii.) Expectoration from canula becomes more or less abundant or sticky, or even purulent if the patient live long enough. (iv.) The dyspnœa follows one of two courses: (α) Either it recurs, and becomes as great as before, so that nothing whatever is gained by having substituted, by means of tracheotomy, pulmonary for laryngeal dyspnœa. Consciousness being retained, the patient suffers as much distress after the tracheotomy as he suffered before it. (β) Or vital debility prevails, there being no great dyspnœa, but the respiration becoming very frequent, and the pulse very small and weak. Lividity steadily increases. The animal constitution soon suffers; drowsiness ensues, the patient being almost continually asleep unless disturbed by cough; sleepiness passes into coma and death, which is easy and without dyspnœa.

Tracheal Diphtheria. — Now and then a case will be met with in which the disease is almost limited to the trachea.

The tracheitis is not primary, but is preceded by a diphtheritic affection of the fauces or larynx, which may have been slight or severe. (i.) The primary sore throat may be attended by the least possible exudation, and the laryngitis be indicated by nothing more than a little

hoarseness, and perhaps a few shreds of false membrane seen by the laryngoscope. In about seven days from the first signs of illness the patient begins to expectorate casts from the trachea. (ii.) Or, after a severe and regular attack of diphtheritic angina and croup (which will in some cases have rendered tracheotomy necessary), the patient seems to be fairly convalescent, when the disease relapses in the tracheal form, expectoration of false membrane occurs, but no recurrence of angina faucium or of laryngitis.

This tracheal diphtheria often deserves the name of chronic, the patient expectorating casts of the trachea from time to time for two months or even longer from the beginning of the disease. Albuminuria, amblyopia, and paralytic symptoms may occur. The prognosis is doubtful; some patients die in one way or another, and some survive.

Diagnosis.—1. Catarrhal laryngitis (catarrhal croup) and diphtheritic laryngitis cannot be distinguished during life unless false membrane be coughed up, or be seen upon the larynx or fauces. Catarrhal croup is never fatal, however severe the dyspnœa be for a time, unless the inflammation spread to the bronchi so that the patient really dies from suffocating bronchitis. A case of croup which becomes steadily worse is probably diphtheritic. But, on the other hand, what seems to be catarrhal croup may be diphtheria in its slightest form.

2. The respiratory stridor in some cases of catarrhal croup is excessive, and reaches a height of noisiness which is uncommon in diphtheritic croup. This stridulous laryngitis is especially apt to occur in measles just before the rash comes out; the dyspnœa and distress of the patient are great; the rash appears, and the croupy symptoms speedily subside. The croup which occurs in measles from four to fourteen days after the appearance of the rash is a more serious disease; it often renders tracheotomy necessary, and is usually laryngeal diphtheria.

3. Spasmodic croup (spasmodic laryngitis, Millar's acute asthma for the most part) is distinguished from other kinds of croup on account of a peculiarity in the course of the dyspnœa. The onset (as in all sorts of croup) is marked by dysphonia and stridor. Dyspnœa soon follows and attains a high degree, especially in the middle of the night. After urgent dyspnœa has lasted from half an hour to two hours it begins to abate, and soon becomes slight, the dysphonia and stridor continuing. Such attacks of dyspnœa are prone to recur for two or three nights in succession, each fit being less severe than the foregoing. Now and then (but very seldom) diphtheritic croup will take on the spasmodic form, wherefore it is prudent not to be too confident in pronouncing at first upon the benignant nature of spasmodic croup. Laryngismus stridulus cannot possibly be mistaken for diphtheritic croup.

4. When a child has inhaled a foreign body which sticks in the larynx, and when the history of the occurrence of the accident is wanting or untrustworthy, it is easy to mistake such a case for croup. It will hardly be possible to gain any help from the laryngoscope. At the instant of the foreign body entering the glottis urgent dyspnœa occurs, so

that an attack of laryngismus is simulated, and the patient may die on the spot. But if he survive the dyspnœa abates, and then the case simulates croup. The diagnosis sometimes cannot be made until after tracheotomy by exploring the larynx by means of a probe passed upwards through the wound.

5. Exacerbations of dyspnœa occurring in children suffering from pectoral diseases, such as hydrothorax and acute pulmonary consumption, sometimes strongly simulate croup; and the more so when the dyspnœa is attended by a husky cough.

6. In the case of adults the diseases most likely to simulate laryngeal diphtheria are sundry forms of laryngitis, œdema glottidis, laryngeal paralysis coming on suddenly, and hysterical laryngismus. But in adults the laryngoscope is available.

Treatment. — Inasmuch as we cannot apply germicides to the air-passages, and as we possess no antidote to diphtheritic poison in the blood, it follows that for us no direct specific treatment of laryngeal diphtheria is possible.[1] Moreover, very little, short of tracheotomy, can be done to mitigate the most distressing symptom. To surround the patient with pure, warm, and somewhat moist air would seem to be indicated by common sense. The only local application which can be recommended is that of ice or of ice-cold water to the front of the neck. Emetics are best avoided; they empty the stomach of food, and any good they may do to the dyspnœa is very temporary; usually they do no good at all.

When the dyspnœa becomes considerable the remedy of tracheotomy must not be deferred too long. It removes the laryngeal dyspnœa, but lividity often persists, and pulmonary dyspnœa often supervenes and kills the patient, as has been already described. Tracheotomy is sometimes followed by evils of its own, for example (i.) Emphysema of the mediastinum, due, according to Dr. Champneys, to the fascia being stripped off from the trachea in the operation. (ii.) Pneumothorax and Mediastinal Suppuration are apt to follow emphysema of the mediastinum. (iii.) Thrombosis, starting from veins injured during the operation, and possibly extending so far as the right auricle. (iv.) Embolism of a large branch of the pulmonary artery, possibly followed by gangrene of the corresponding portion of lung. (v.) Ulceration of the trachea, due to irritation set up by the end of the canula. (vi.) Sloughing of phagedænic ulceration due to septic infection of the wound.

Tracheotomy, although it usually raises the temperature of the body, does not always do so. It is a bad sign when the nostrils act strongly, or when the breathing through the canula becomes sawing or hissing.

Young children after tracheotomy should be fed by means of an india-rubber catheter passed through a nostril into the œsophagus, and the same method should be employed in all cases which show any tendency for the drink swallowed to pass into the larynx.

The tube should be removed as soon as possible, nor is it too early to

[1] Refer to the last chapter upon the Serum Treatment.

make the attempt within twenty-four hours after the operation. But sometimes the tube cannot be removed for a long time after, or, indeed, cannot be removed at all. The cause of the difficulty is not always the same. An abundant growth of granulations sometimes obstructs the windpipe about the wound; this is said to be especially the case when the cricoid cartilage has been divided. Cicatricial contraction of the windpipe above or below the wound is another possible cause of obstruction. The trachea is sometimes dislocated backwards, so that the channel of the windpipe below the wound is not continuous with that above. But in many cases it is hard to say what the cause of the difficulty is, and little or no help can be gained from the use of the laryngoscope. Paralysis of the glottic dilators is an explanation possible in some patients; in some the emotion of fear seems to play a large part in aggravating any distress which follows removal of the tube. In many of these doubtful cases time alone will suffice to cure.

The use of tubage or intubation of the glottis is a topic which hardly needs to be discussed with reference to diphtheritic laryngitis. In this disease tubage is not a reasonable method of treatment unless, in a given case, we know that the exudation is confined to the larynx and will not spread beyond it.[1] But these are certainties to which we cannot attain, and in practice we have nothing more to guide us than probabilities which may be high or which may be low. If we can believe that the croup is not membranous, or that, if membranous, the disease does not extend below the larynx, we may be disposed to try intubation, but always with the prospect of having to perform tracheotomy afterwards. My own opinion is that tracheotomy should be preferred in all cases. Difficulties and dangers attend tracheotomy, and tubage is not free from them. What are called statistics are of little value in determining the relative merit of the two operations, and are of no value at all, if among successful intubations are to be reckoned cases in which the tube passed out per anum.

C. Nasal Diphtheria

Diphtheritic membranes in the nose are often associated with diphtheria of the fauces, a combination which usually indicates a severe form of the disease, but not always. Very slight pellicular sore throat, so slight that its diphtheritic nature is doubtful, may be attended and followed by puriform discharge from the nose, the patient in all other respects seeming to be in good health; and yet this discharge will be capable of conveying diphtheria to other people. Still the rule is, as aforesaid, that diphtheria affecting both throat and nose is malignant or pestilent diphtheria.

Diphtheria sometimes affects the nose alone, so far as can be made out. The sign of this form, as of all forms, of nasal diphtheria is stuffing

[1] See the last chapter on the Serum Treatment.

of the nose and a puriform discharge, sometimes offensive, sometimes bloody, and often very irritant to the nostrils and upper lip. The hæmorrhage is sometimes sufficient to weaken the patient, or even to be the cause of death. The redness and swelling may spread from the nostrils so as to affect the whole nose and the eyelids. The swelling is sometimes attended by erysipelatous redness of the skin. Yet it may happen that there shall be no discharge, and stuffiness be the only sign of nasal disease. Very seldom do membranes come away so as to be discovered in the discharge; they can sometimes be seen by inspection of the nasal fossæ, more commonly they are limited to the hinder parts of those cavities.

The glands at the angle of the jaw tend to be swollen, tender, and painful. Should one nostril alone be affected the glands will be enlarged upon the same side.

The general symptoms of diphtheria confined to the nose are usually marked enough, but they are often supposed to be due to a common cold in the head, and are not much attended to. Albuminuria is usually present during the time of the nasal discharge, and even for some time afterwards. Paralysis will follow in some cases, and may present this peculiarity, that the fauces are not affected even although the limbs suffer severely.

Nasal diphtheria is to be treated upon the same principles as faucial diphtheria.

D. Other Local Forms of Diphtheria

Otitis media is sometimes diphtheritic, and false membranes are found in the tympanum after death. The amount of associated faucial disease may be considerable or may be slight, even so slight that its nature is doubtful. The signs of otitis are the same as those of other forms of the disease. The diagnosis depends upon the discovery of diphtheria elsewhere. Erysipelas of the ear and neighbouring parts sometimes follows upon rupture of the tympanic membrane. Chronic otorrhœa may ensue.

A portion of the skin which is excoriated or blistered is prone to be attacked by diphtheria in a patient already suffering from that disease; the membrane, if thick, looks very much like a layer of lard. The skin around is often erysipelatous.

A granulating wound is very seldom attacked, the wound of tracheotomy often becomes foul and phagedænic, but anything like false membrane is rarely or never seen.

Conjunctival diphtheria (which is said to be sometimes due to the disease spreading up the lachrymal passages), and diphtheria of the vulva, vagina, anus, or prepuce, are diseases very uncommon in England.

The œsophagus is seldom affected. This form of disease affords no characteristic symptoms, and is usually not suspected during life unless a membranous cast be rejected.

Diphtheria of the stomach has been referred to in the chapter on vomiting.

E. Latent Diphtheria

The diphtheritic poison may affect the throat without being revealed by the formation of false membrane. In this case the mucous membrane is either red, swollen, tender and painful, or it looks quite natural. The former condition cannot be distinguished from simple inflamed or catarrhal sore throat, unless there be good reason for believing that the patient has been exposed to the operation of the diphtheritic poison, unless the specific bacillus be found in the secretions, unless the patient convey diphtheria to some neighbour, or unless the peculiar paralytic symptoms follow what seemed to be a common sore throat. After a manifest attack of diphtheritic angina faucium the throat may seem to have returned to its normal condition, and yet the microscope may discover the specific bacillus in the secretions, even after a considerable time (seven months it is said) has elapsed since the cessation of the disease.

Diphtheria of the larynx is often latent; that is to say, a patient has croup, and from first to last it is impossible to say whether the disease be diphtheritic or not.

Latent nasal diphtheria is either primary or secondary: (i.) A patient has a discharge from one or both nostrils, which is deemed at first to be a simple coryza, and which, if the disease last several weeks, is supposed to be due to syphilis, disease of the turbinate bones, or of the maxillary antrum; and surgical proceedings may be recommended. But the debility of the patient is noted to be greater than the local disease can account for, or the urine is found to be albuminous, or paralytic symptoms occur, and thus the true nature of the disease becomes apparent. (ii.) The latent nasal diphtheria which is secondary to a manifest attack of the disease has been already described.

S. Gee.

Serum Treatment

As explained elsewhere [see art. on "Serum Therapeutics"], in certain diseases the blood serum of artificially protected animals, if injected into others still susceptible, has a protective power; and Behring conceived the idea that a similar treatment might be adopted in diphtheria (1). He found that it could be used not only as a protecting agent, but also as a cure (2), and after many trials he succeeded in producing a serum strong enough to be of use for man. From that time to this modifications have continually been introduced by Behring himself and by others, which have enabled us to produce stronger and stronger preparations of the serum: to describe these in detail is beyond the scope of the present article. To Aronson we owe the employment of horses, from which animals the serum now in use is obtained.

The new remedy was first employed, and the first accounts of its

effects were published by Berlin physicians (3, 4). Their results were confirmed in Paris by Roux, and by other physicians in Germany. Since then it has been used all over the world.

It is unnecessary now, and will probably be still less needful when these words are published, to quote at length the great number of clinical and statistical papers on which our judgment has been formed. They have been collected and excellently analyzed up to July 1895 by Welch. No one man has published finer work upon the subject than Baginsky, whose book, besides resting on a larger number of cases than has fallen to the lot of any other physician, contains the most cogent proof of the value of the serum ever yet brought forward. Between 15th March 1894 and 15th March 1895 he treated by the antitoxin 525 children up to fourteen years of age, of whom 83, or 15·6 per cent, died. The supply of serum failed about August and September, and during that time 126 children were treated without the antitoxin, of whom 61, or 48·4 per cent, died. When the serum was resumed the mortality at once fell again. The higher rate is about the level of previous years.

At the Eastern Hospital in London (8), from 1st January 1893 to 22nd October 1894, 797 patients under fifteen years of age were treated by the old methods, of whom 310, or 38·8 per cent, died. From 23rd October to 27th November 1894, 72 such patients were treated by the antitoxin, of whom only 14, or 19·4 per cent, died.

At St. Bartholomew's Hospital (9) we treated, during 1893 and the first part of 1894, 95 cases under ten years of age with 50 deaths, a rate of 52·7 per cent. Between 1st July 1894 and 8th July 1895, 50 cases of the same age were treated with the antitoxin, of whom only 8 died, a rate of 16 per cent. This fall in the death-rate must be a little discounted; first, because proportionately more patients were admitted in the first three days after symptoms were noticed; and, secondly, because proportionately fewer patients were admitted under two years of age during the second period than during the first. But the difference thus made is, when calculated, slight, and if by grouping like cases with like the numbers are more closely compared, the value of the serum is more clearly shown. Thus, of cases in which the diphtheria affected together with other parts the nose —

During the first period 28 died out of 39
" second " 3 " " 12

Of cases in which both fauces and larynx, but not the nose, were affected —

During the first period 16 died out of 39
" second " 4 " " 20

Of tracheotomy cases —

During the first period 39 died out of 67
" second " 6 " " 32

Most physicians agree that under this treatment the local symptoms clear up with much greater rapidity than of old. That the disease is

also robbed of its power on the constitution is proved partly by the great fall in the death-rate and partly by clinical observation. It does not, however, appear to influence the temperature (9), and whether paralysis occurs less often now is still doubtful. Hayward (9) found that of the above 50 cases only 2 showed any trace of paralysis; however, the number is but small, and, moreover, the average rate of incidence is an unknown quantity. No hospitals retain their patients long enough to settle the question, and I have had many out-patients suffering with these symptoms who had been discharged from hospitals as cured. Albuminuria is certainly not more — in our case it was rather less — frequent under this treatment, and the same is true of nephritis.

Dr. Gee thinks it probable that intubation will now be of more use than hitherto. The great objection to intubation has been that it affords no egress for the membranes continuously formed in the trachea. If by serum we can stop the formation of membrane the objection ceases to be valid.

In some cases the injection of the serum is followed by a rash, erythematous or urticarious, upon the skin [see also art. on "Serum Therapeutics"]. In a few cases there is itching, but it has no other ill effect, and it passes off sometimes within a few hours, sometimes within a few days. Less often — we have never seen it — there is pain and swelling in some of the joints, which is also transient. Both these effects are due rather to the serum than to the antitoxin — whatever that may be — which it contains; and the smaller the dose of serum the less likely are these symptoms to occur.

The injections are best made deeply into the buttock. The syringe must be such that it can be perfectly sterilised by boiling, and should hold at least 10 c.c. It is best to connect it with the needle by an india-rubber tube. The whole should be boiled before each injection, and the skin washed first with soap and water, and then with a $\frac{1}{20}$ solution of carbolic acid. The puncture should afterwards be covered with a small piece of isinglass plaster, or similar protective [see art. on "Serum Therapeutics"]. The dose varies with the different preparations of serum. Of Klein's serum, which we are now using at St. Bartholomew's Hospital, we give 5–8 c.c. once or twice daily for several days, or even oftener, according to the severity of the case. In serious cases the treatment must be pushed to get the full effect immediately, or as quickly as possible. Especially where there is broncho-pneumonia the injections should be practised energetically; for Dr. Kanthack and Mr. J. W. W. Stephens have shown that in such cases the lungs generally, if not always, contain the diphtheria bacilli in enormous numbers; in other words, the amount of poison to be rendered harmless is very considerable (*vide supra*). The strongest serum is the best.

W. P. Herringham.

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W. P. H.

TETANUS

Syn. — Greek, τέτανος (a straining, from τείνω); Latin, *Rigor Nervorum* (Celsus); Germ., *Starrkrampf.*

Tetanus may occur in any person of either sex, at any age; it may ensue from any wound at any part of the body, and in any condition of the wound; or without any apparent wound. It less often follows wounds of the trunk than of the extremities, and wounds of the lower extremities give rise to it more frequently than those of other parts; but it does not appear that wounds of the feet or hands are more liable to cause it than those of other parts of the limbs. On the whole, however, it occurs more frequently in parts exposed to contact with earth and dirt. How the popular but mistaken idea arose that it has any especial relation to injuries in the region between the thumb and the forefinger is not easy to tell. It is most likely to occur in cases of severe or lacerated wounds, or when some foreign body is lodged in a simple incised wound, or in compound fractures or burns. It may ensue upon a mere scratch; the slightest wounds, such as those caused by subcutaneous injections; dilation of the neck of the uterus by a sponge-tent; after confinements (the post-parturient cases are said to be especially fatal); after cupping; the insertion of a seton; the extraction of a tooth; the injection of a hydrocele;[1] or the plugging of a nostril for epistaxis. In a woman in Addenbrooke's Hospital the only discoverable local lesion was a chronic ulcer of the leg. It has also been known to take place after complete cicatrisation of the wound (4). In horses it is said to be caused by wounds in the gums from eating straw; and cases supposed to be idiopathic may have originated in this way. It is liable to follow exposure to cold and a damp, chilly atmosphere, as in the cases of wounded soldiers lying upon the field of battle. In an early case of ovariotomy in the country, long before the days of antiseptic surgery, all had gone on well, the wound had nearly healed, and I had taken my leave of the patient, when tetanus supervened and proved fatal. I witnessed another fatal case after ovariotomy, with antiseptic precautions, performed by the late Dr. Meadows. I judge that the disease has been less frequent since the introduction of the antiseptic method in the treatment of wounds; and we may hope that this immunity will be still more observable as the new methods are more generally and completely carried out, and a more thorough cleansing and quicker healing of wounds effected.

For obvious reasons the disease is more frequent in men than in women, and it is said to be less fatal in women. I have seen three cases in women, and it proved fatal in all. One female infant, whose case is subsequently mentioned, recovered. It is most frequent between the

[1] Gross relates that in a lad who had a bruised chin with a small ulcer on the tongue probably caused at the same time, and who died of tetanus, a large hydatid was found in the liver.

ages of ten and twenty, and is rare after sixty (20). It is much more common in warm countries than in temperate regions, which is somewhat remarkable, seeing that its occurrence in the latter is often attributable to exposure to cold and damp. It sometimes occurs as an epidemic. Gross says (I do not know upon what authority) that in 1858 it appeared in rapid succession in several of the London hospitals. Macnamara (5) states that in Bengal tetanus has been observed to occur especially after changes of temperature, and that it is rarely absent from the hospitals of Calcutta. He adds that within a period of five years 83 cases were treated in the surgical wards of the Mayo Hospital; of these 44 were traumatic, and 24 (a small proportion) died: of the remaining 39 idiopathic cases 10 died (3, 21). It is more frequent and more fatal in military than in civil practice. The records, however, of the "Great Rebellion" (see appendix) are more favourable than those usually given of the results in civil practice.

G. M. H.

Pathology. — Although it is only within recent years that any proof of the bacterial origin of tetanus has been forthcoming, this disease has for some time been classified by surgeons amongst the specific infective fevers of septic origin. Perhaps one of the most remarkable foreshadowings of the exact nature of tetanus is given by Sir James Simpson who, writing in 1854, says: "Tetanus is known to follow wounds very various in their degree of severity. . . . The disease, when developed, essentially consists of an exalted or superexcited state of the reflex spinal system, or of some segment or portion of that system." He then goes on to say, "We have in obstetric pathology evidence almost amounting to certainty that the analogous superexcitable state of the cerebro-spinal system of nerves which gives rise to eclampsia or puerperal convulsions is generally produced by the existence of a morbid poison in the blood. And it seems not impossible that the generation of a special blood poison, at the site of the wound or elsewhere, may sometimes in the same way give rise to obstetrical and surgical tetanus." He further pointed out that the symptoms of this disease are comparable to those produced by strychnine and brucine. It was, however, found impossible by clinical observation to determine the nature of this poison, and it was not until several years after the publication of Koch's experiments on septicæmia that this poison was proved to be the result of the activity of a micro-organism which had found a nidus in injured tissues.

Most of the earlier experiments were directed to the discovery of micro-organisms in the blood, in the lymphatics around a wound, or along the course of the peripheral and central nerves. Simpson says that attempts had been made even before his time to reproduce the disease experimentally by injections of the blood of patients who had succumbed to tetanus. But all such attempts were fruitless, and the matter was eventually settled by a very different line of experiment.

Carle and Rattone, in 1884, discovered a virus in tetanus that could

be inoculated from man to animals (of twelve rabbits inoculated, all except one were attacked); they regarded this virus as a *contagium vivum*, probably a bacterium. In the following year Nicolaier published his dissertation, in which he recorded his success in obtaining from pus a virus which he was able to propagate outside the living organism; he also found that certain animals, such as rabbits, guinea-pigs and mice, when inoculated with particles of soil obtained either from the streets or from cultivated land, became affected by symptoms which he described as tetanic in character and as identical with those observed in man. This soil, introduced into a little pocket under the skin, was almost invariably followed by an abscess. The pus in this abscess was found to contain several species of micro-organisms, one of which (although he carried on cultivations for seven generations he could never obtain absolutely pure) he identified as being specially active in setting up tetanic convulsions. He described this organism as a small, slender bacillus, somewhat longer but thinner than Koch's bacillus of mouse septicæmia, but he gave no further specific features of identification. In 1886 Rosenbach corroborated and established Nicolaier's observations, by inoculating two guinea-pigs with pus from a tetanic patient, which produced tetanic muscular contraction like that invariably produced by the inoculation of Nicolaier's earth. Rosenbach also produced evidence that one of two bacilli was probably the cause of the tetanic condition: (*a*) a rapidly-growing, thick bacillus, which developed large spores, and had the power of peptonising serum; (*b*) a slender bacillus, which first appeared in the liquefied serum, and then formed spores. He agreed with Nicolaier that the tetanus bacillus was probably the small and slender organism.

It was not till 1889 that **the tetanus bacillus** was obtained in pure cultures by Kitasato, and also by Tizzoni and Cattani, who were able to separate the specific tetanus organism, as at present recognised, from the pus of the abscesses occurring in cases of tetanus, and from the tissues immediately surrounding these abscesses. Knud Faber, in investigations carried on about the same time as those of Kitasato, although not successful in obtaining a pure culture of the tetanus bacillus, states that his experiments support Kitasato's view that the organism is an obligate anaerobe. He was the first to obtain by filtration of very virulent tetanus cultures a perfectly germ-free filtrate which, when inoculated into animals, reproduced the whole of the disease phenomena of experimental tetanus.

The organism described by these authors, and now recognized as the specific cause of tetanus, usually occurs as delicate threads, and it varies in length from 4 μ to 5 μ long, to but slender threads; these are slightly thicker than the bacillus of mouse septicæmia (one of the smallest organisms known), and the ends are somewhat rounded. In the shorter rods, which are non-motile during this stage, spores usually make their appearance at blood temperature in about thirty hours after multiplication has commenced; but at the temperature of the room they are not observed until about a week has elapsed from the commencement of the growth, although the organism con-

tinues to grow readily enough at this temperature. Until the spores begin to form the threads are usually motile, and the segmentation into short rods may be incomplete; but as soon as sporulation commences the segments become more perfectly marked out, they become motionless, and a clear point is observed at one end of the rod; this becomes larger and larger until it causes marked distension of the end of the bacillus in which it is developed, and thus is formed what is known as the "pin-head" or "drum-stick" bacillus. This organism grows best at a temperature of from 36° C. to that of the blood. Below 14° C. it becomes inactive: at 42° C. to 43° C. it also becomes less active, and undergoes what are looked upon as degenerative changes, involution forms being pretty constantly developed; and exposure to a temperature of from 60° C. to 65° C. rapidly kills off the bacillus, but does not destroy any spores that may have been formed. These spores are exceedingly resistant, even to moist heat, as they can withstand the action of water at a temperature of 80° C. even for an hour; whilst steam at a temperature of 100° C. does not appear to be fatal to them in a less time than five minutes. It is also stated that it requires fifteen hours of treatment with a 1 in 20 watery solution of carbolic acid, or three hours with a 1 per 1000 corrosive sublimate solution, to kill them. Protected from air and light the spore may retain its vitality for as long a period as twelve months, at the end of which time it still appears to be capable, under certain conditions, of developing into the vegetative form. The tetanus bacillus is anaerobic, and grows best in an atmosphere of hydrogen; it appears, however, to be almost as inactive in the presence of carbonic acid gas as in the presence of more than traces of oxygen.

This bacillus is stained by Gram's method. The spores are best stained by leaving them for some time in a 10 per cent alcoholic solution of basic fuchsin, 10 parts, added to 100 parts of a 5 per cent watery solution of carbolic acid. The specimen may be left in this stain for about twelve hours; or the same result may be obtained in two or three minutes if the solution be heated until steam rises from it. The bacilli give up the stain in 25 per cent solutions of mineral acids, but the spores retain it firmly. A contrast stain is obtained by placing the specimen for a couple of minutes in a watery solution of methylene blue.

The tetanus bacillus has been found in garden earth, in dust from the streets, between the boards of the floors of rooms, and in the pus from certain suppurating wounds. It has also been met with in the excrement of animals, especially of the horse. Marchesi found that samples of soil freshly gathered often give rise to mixed infections in which tetanus poison may not appear to play a part; but if to the same soils he added a 5 per cent solution of carbolic acid (which appears to kill most other organisms), he could usually demonstrate their tetanising power; other infections seldom or never occurring. By using this method he has been able to produce tetanus symptoms, not always at the first attempt but often on the second; and he points out that the absence of an infection after the first inoculation does not necessarily show that a soil

contains no tetanising organisms. He has found tetanus bacilli to a depth of two metres; but, below that, soils examined by him had not the power of inducing tetanus when inoculated subcutaneously.

It always occurs, then, in these positions along with other organisms, and, from the fact that it grows anaerobically, it had, as we have seen, been known to exist for five years before any one succeeded in obtaining it in pure culture. Kitasato, however, at last overcame the difficulty by taking advantage of the fact that the spores of this organism are specially resistant to the influence of heat. Taking as his seed material some of the pus from the wound of a patient suffering from tetanus, he made cultures on the surface of agar-agar. At the end of a couple of days he found a number of organisms developed on the nutrient medium kept at the temperature of the body; and amongst these were characteristic tetanus bacilli. He then exposed some of the mixture for one hour to a temperature of 80° C.; from the material so treated he made fresh anaerobic cultures, and in a certain proportion of these he was able to obtain pure groups of the tetanus bacillus. It should be pointed out, however, that certain anaerobic bacilli, which may even be mistaken for the tetanus bacillus, except that they do not give rise to a similar poison, may form spores which are equally resistant to the action of heat. This admixture most frequently accompanies the tetanus organism when it occurs in soil; but, as a rule, we are not met by the same difficulty when the cultures are made directly from purulent material derived from tetanus cases.

The bacillus, as we have seen, grows best at the temperature of the body, and anaerobically. It certainly retains its virulence only so long as the free access of oxygen is interfered with; but it is stated that constant cultivation in an atmosphere of pure hydrogen also, to a certain extent, interferes with its virulence.

It grows readily on any of the ordinary media to which an addition of 2 to 3 per cent of grape sugar is made, even when oxygen is present at the surface of the mass. In gelatine plates at the temperature of the room there are seen at the end of about four days small, slowly growing colonies with delicate marginal processes. Under the microscope each colony appears to have a dense centre whilst the margin is clearer, and radiating from the main mass are numerous exceedingly fine threads. In stab-cultures in gelatine, kept at a temperature of 21° or 22° C., a growth makes its appearance in the deeper part of the gelatine in the form of a fir-tree, situated some little distance from the upper surface of the medium, the gray, delicate, fluffy-looking branches getting longer and longer as the surface is left. At the end of the second week the gelatine begins to liquefy, and this liquefaction continues until the whole becomes a cloudy, sticky fluid. After a time the growth sinks to the bottom, leaving the upper part of the gelatine comparatively clear. There is a similar growth in grape sugar agar; but as this medium can be kept at the temperature of the body, the growth goes on much more rapidly, and is of course not accompanied by liquefaction. It is a dis-

puted point whether gas bubbles are formed under these conditions or not. This appears to be entirely a question of the rate of formation of gas; if it is formed more rapidly than it can be diffused through the agar — as in the case of very energetic growth — bubbles may be seen; but this, in my experience, is comparatively rare, and the presence of gas bubbles affords strong evidence of the impurity of the culture. In grape sugar peptone bouillon the organisms grow luxuriantly, especially at the temperature of the body, and the fluid rapidly becomes cloudy; but after a lapse of six or seven days the upper layers of the fluid become clear, and a grayish white mass falls to the bottom of the tube. All these cultures have a peculiarly disagreeable aromatic odour.

The Tetanus Bacillus is a Facultative Parasite. — It grows outside the body, and is especially associated with the stable and with manured fields. Sheep and cattle are often affected. The disease is most common amongst agricultural labourers, gardeners, soldiers on campaign, in those who go about with bare feet, or who, like young children, are liable to get their knees or hands accidentally wounded by contact with the ground. It is somewhat important to remember these facts, as it has been found that the tetanus organism only retains its virulence under cultivation so long as it is grown under anaerobic conditions; especially is this the case where there has been no time for spores to develop themselves. Even the pus from wounds of a patient suffering from tetanus may no longer be capable of setting up tetanus infection, as the bacilli are often there placed under conditions unfavourable to the retention of their specific virulence.

Inoculation. — This infective process may be set up in the smaller animals by the insertion under the skin of minute particles of almost any cultivated garden earth; by inoculation of pure anaerobic cultures of the tetanus bacillus; by the inoculation of a pure culture plus the tetanus poison, or plus lactic acid or bacillus prodigiosus; or by inoculation into a bruised wound. It is worthy of note, however, that the older the culture and the more poison there is present, the greater the certainty that the disease will follow inoculation. It should be remembered that the tetanus bacillus forms its poison exceedingly slowly, and that the organisms themselves, if unaccompanied by any material which will, as it were, draw off the attention or paralyse the activity of the tissue cells, are rapidly destroyed by these cells — so rapidly, indeed, that they have no time to form sufficient poison to set up the nerve changes associated with the disease. Slowly as the poison is formed, however, it is tremendously active, as will readily be supposed when I say that the five-millionth part of a cubic centimetre of a filtered two to four weeks old slightly alkaline broth culture of the tetanus bacillus — that is, of a solution of the poison formed by these organisms — is sufficient when inoculated subcutaneously into a mouse to kill that animal in twenty-four hours. The lethal dose for a rabbit is about a thousand times this quantity; for dogs five to ten thousand times; and for fowls and pigeons ten to twenty-five thousand times of an even stronger fluid.

Tetanus may be produced in frogs, but only, it appears, when their temperature is maintained at a higher point than normal: the period of incubation usually extends over a period of two or three weeks. Unlike the poison produced by many other organisms, that of the tetanus bacillus seems to produce much the same results whether it be injected subcutaneously into the thorax or abdomen, or into the veins. This bacillus appears never to attack an animal from the alimentary canal.

In experimentally produced tetanus the spasms are first observed in the muscles near the site of inoculation; but ultimately the process may become general. After intra-peritoneal and after intra-venous injection, however, there is usually a general infection from the commencement. In many cases the changes at the seat of inoculation may be so slight as to be overlooked unless carefully searched for. This point is of special importance as many cases of tetanus are said to be idiopathic; in these, however, it is probable that the initial local damage has escaped observation. Even in experimental tetanus there is as a rule only slight infiltration at the seat of inoculation. This *absence of local manifestation* significantly indicates also that the tissues at this point are incapable of reacting, and that the poison has been rapidly absorbed from the point of introduction. It is only when mixed cultures are injected, or cultures mixed with other foreign bodies, such as pus, pieces of tissue from a wound, soil, etc., that a local suppuration takes place.

The tetanus bacillus, or its spores, when introduced alone does not set up suppuration. Vaillard points out in connection with this class of case, that in one of his animal experiments, in which he had introduced spores under the skin, the wound healed immediately. For some time no symptoms of tetanus arose; but when later the wounded limb was irritated the spores became active and an attack of tetanus was the result. In those cases where tetanus is propagated in wounds treated antiseptically, it must be assumed that spores which have not been killed by the antiseptic agents have remained latent in the healing tissues for some time. Later they have developed into bacilli, have commenced the manufacture of their toxins, and so have induced an attack of tetanus.

Vaillard and Rouget, along with Vincent, state that spores of the tetanus bacillus from which all traces of poison have been removed by careful washing, when inoculated alone into an animal, are incapable of setting up tetanus. Klipstein, on the other hand, maintains that this washing of the spores injures them so seriously that they certainly lose a great part of their infective property, but that this infective power is never entirely lost. Vaillard and Rouget, however, are satisfied that their own observations are correct. It is certainly a fact that in many cases pure cultures of tetanus bacillus fail to set up a tetanic infection; but this may be due to the activity of the tissues, as equally well-marked failures may be observed in the infective agents of other diseases.

Speaking generally, tetanus follows so distinctive and regular a course that it may be divided into three stages (Knud Faber) — (*a*) *the*

incubation period, (b) the stage in which local spasms are developed, and (c) the stage in which we have general tetanic convulsions. In certain of the smaller and very susceptible animals the incubation period extends over a comparatively short time, especially in the case of the experimentally produced disease. For instance, in mice inoculated with pure fluid cultures of the tetanus bacillus, the incubation period may be as short as five or six hours, though it may be as long as from twenty-four to forty-eight hours. When earth is used the incubation period is somewhat longer, and is usually put down at from two to three days. In the guinea-pig the incubation period is slightly longer, being usually from one to two days. There is some difference of opinion as to the period of incubation in the rabbit. Knud Faber describes the incubation period in this animal as being from twenty-four to forty-eight hours; other observers place it at from eight to fourteen days. There can be no doubt that the period of incubation varies considerably in rabbits according to the dose administered and the size and age of the animal experimented upon. Trismus, which is a marked feature in the rabbit when the incubation period is short, is seldom observed in the mouse and the guinea-pig. After injection of very virulent cultures the general tetanic convulsions, as seen in the mouse, are never observed in the rabbit. A most important point observed by Knud Faber is that there is not a gradual transition from the local spasm into the general tetanic convulsions, but a sharp line of demarcation between the two; the general muscular spasm beginning as an entirely new phenomenon perfectly distinct from the local symptoms. The disease in the rabbit is specially interesting, because in it the disease manifests itself much as it does in the human subject, both as regards the non-fatal form of the disease, in which merely local spasms are developed, and the malignant type, which begins with local spasms, and passes on to trismus and stiffening of the neck; when an intra-venous injection of the virus is made a general tetanic condition may be produced corresponding in almost every detail with that seen in the human subject. In the human subject the period of incubation is of course somewhat longer, from one to twenty-two days; in the frog, as we have seen, this period of incubation is from one to two weeks.

On examination it is found that the tetanus bacillus is localised entirely in the region of the seat of inoculation: it is never found in the blood or fluids of viscera, or in distant tissues; and no changes are demonstrable in the various organs. Hence the failure of earlier experimenters to produce the disease by the injection of blood from tetanic patients. Tetanus, then, is essentially a toxic infective process, the poison being absorbed from the seat of inoculation, where it may have been originally introduced in sufficiently large quantities to bring about the characteristic tetanic symptoms in a very short time; or the tetanus organisms may there be so favourably situated that they can develop a sufficient quantity of their products to set up toxic symptoms: the bacilli are distinctly localised, but the poison may be widely diffused. Kitasato

and Knud Faber, working independently, pointed out that the whole of the phenomena of a fatal attack of tetanus could be induced by the injection of the poison quite apart from the bacilli by which it was formed. Kitasato inoculated mice at the root of the tail with cultures of the bacillus; and after a half, one, and one and a half hours respectively, he cut freely around the inoculation wound and carefully cauterised it, thus removing all the bacilli that he had introduced. He found, however, that only the animals in which the parts were removed at the first of these intervals escaped an attack of tetanus; from which he argued that the poison formed by the bacilli is the essential factor of the disease in experimental tetanus, and not the bacilli themselves. Vaillard and Vincent, who repeated these experiments, obtained much the same results.

Most cases of **accidental traumatic tetanus** differ materially from cases experimentally produced, in that other organisms and foreign bodies are frequently introduced with the specific bacillus; suppuration is set up, and under these conditions this bacillus appears to have peculiar powers of developing its poison. It is sometimes held that the tetano-toxin is produced for a time only, and that the development of the bacillus is soon arrested, even in cases that ultimately succumb to the disease; but Roux and Vaillard maintain that this is not the case, and that before a case of tetanus can be treated with any degree of success the infective focus must be freely removed so that the supply of toxin may be cut short. So long as bacilli continue to multiply in the wound they are probably producing poison; and therefore every attempt should be made to cut short their increase. The point of entrance of tetanus virus is usually a wound which may be at the outer surface; say, of the uterus shortly after childbirth, or in the severed cord of new-born children. Patients, as we have seen, are usually affected when working amongst horses, or when wounded while following agricultural pursuits. It is maintained, indeed, that the horse is the natural host of the tetanus bacillus, which is found in and spread with the dung of this animal.

The tetanus poison resembles the enzymes in many respects; it is destroyed at a temperature of 65° C. in about five minutes: if kept at the temperature of the body for any length of time it gradually becomes weakened. When kept on ice, and protected from the action of light, it retains its poisonous properties, unchanged, for months. By the addition of 0·5 per cent carbolic acid, or of an equal volume of glycerine, it may likewise be preserved for some time. It is not affected by drying at ordinary temperatures; but owing to its great instability in the presence of most of the ordinary chemical reagents, it is an exceedingly difficult matter to obtain this poison as a pure substance. Brieger first isolated three substances — tetanin, tetano-toxin, and spasmo-toxin — by means of which tetanic symptoms, and in some instances death, could be induced in animals; but these substances had to be given in doses of such enormous volume that it is evident that none of them can be the essential poison of tetanus which acts in the extremely minute doses described on p. 763. Kitasato and Weyl obtained two ptomaines, one very slightly

toxic, which they named chlorhydrate of tetanin, the other a tetano-toxin compound which produced paralytic symptoms. Brieger and Fränkel then described a proteid poison which they obtained from cultures of the tetanus bacillus, and named tox-albumin; they obtained it by saturating with alcohol the fluid in which the organism had grown, whereupon a precipitate having an extremely powerful action is thrown down. It was maintained, however, that this albuminous precipitate simply serves as a kind of network in which the essential toxic substance is entangled; and Knud Faber, Tizzoni and Cattani, and Vaillard and Vincent, affirmed that this poison is probably of the nature of a diastase. Brieger and Kitasato and Weyl then succeeded in obtaining an extremely virulent poison which does not give the reaction for albumins. It consists of yellow, transparent flakes readily soluble in water; it is not destroyed by drying, nor in the dried state by absolute alcohol, chloroform, or anhydrous ether; it is very readily decomposed by acids or alkalies, by sulphuretted hydrogen, and by high temperature: in these features it resembles tetanus poison in its original solution. Its toxic power is represented as being 500 times as great as that of atropin; and 120 to 400 times as great as that of strychnine. Although so much knowledge of the physiological action of this substance has been obtained, very little light has been thrown on its chemical composition. Brieger and Cohn maintain that since tetanus bacilli have the power of producing the poison in non-albuminous media the poison must be looked upon as probably non-proteid. It must be remembered in this connection, however, that the protoplasm of many bacteria has the power of building up proteid substances out of non-proteid foods. The virulence of the poison and the nature of its action upon animals both indicate that it belongs to the enzymes or diastases.

Tetanus in man is accompanied by the same series of processes that have been induced in animals in experimental tetanus. As we have already seen, it occurs sometimes in patients suffering from suppurating wounds, such suppuration being the result of a mixed infection. In man as in animals it is found that the bacilli never pass from the immediate neighbourhood of the seat of the original lesion which, then, must be looked upon as merely the local manufactory of the poison. The toxic products of the tetanus bacillus can, however, be demonstrated in the blood of the general circulation; and in certain comparatively recent experiments tetanic symptoms have been induced in mice by injecting the serum of the blood from a tetanic patient: again toxic products have been obtained from the liver, spleen and spinal cord of patients who had succumbed to tetanus. These toxic products, obtained by throwing down an alcoholic precipitate and dissolving it in water, when injected into small animals have set up all the symptoms of tetanus. The tetanic poison appears to be excreted in the urine and also in the milk.

Bacteriological Diagnosis. — A drop of the pus or other suspected material is inoculated into a subcutaneous pocket just above the root of the tail of a mouse; if the material contain tetanus bacilli the animal

usually succumbs in the course of a few days. Or a small amount of pus taken from the seat of inoculation may be used for inoculating nutrient media to be treated by Kitasato's method. Or again the suspected material may be inoculated into bouillon which is incubated in an atmosphere of hydrogen for three to five days; this broth, with the organisms growing in it, is then placed in a water bath kept at a temperature of 80° C.: here it is left for one hour, after which a fresh anaerobic bouillon culture is made, and this process is repeated until pure cultures of the tetanus bacillus are obtained.

Effect of Tetanic Poison on the Nervous System. — From the fact that muscular spasms are such a constant and striking feature in poisoning due to the action of the tetanus bacillus, and from the fact, too, that the dosage of the poison can be pretty accurately measured, and the living bacilli eliminated from the equation, much experimental work has been done on the etiology and pathology of tetanus; though many points still remain to be cleared up. As regards the pathogenesis of the disease, the earlier researches of Pasteur on rabies led those who were engaged on the investigations to suppose that tetanus is due to the presence and action of some virus which they assumed to be formed in the nervous system, especially in the spinal cord; and that the violent nervous symptoms were induced by the action of this virus. Knud Faber made a number of experiments on inoculation of the nervous centres with the tetanus virus: but, like the experiments of those whose work in this direction had preceded his own, they entirely failed; as did also his attempts to obtain any bacilli from the tissues of the central nervous system even in marked cases of tetanus. On this account he concluded that the virus could not be formed in the central nervous system, as it was evident that the poison could not be formed without the intervention of the tetanus bacilli. Following up Brieger's intoxication theory, Knud Faber was able to show that a pure culture of the tetanus bacillus produces during its growth a poison or group of poisons which, when separated entirely from the bacilli, is capable of setting up characteristic tetanic symptoms. This fact was not entirely new, but it is to Knud Faber that we owe the first observation that the poison only acts after a certain period of incubation, this period depending upon the amount of the poison introduced. He also pointed out that it has many of the characteristics of the diastase or enzyme group, and that we should argue from this period of incubation that it must have time to set up certain fermentive or diastatic changes in the fluids or tissues of the body. He also showed that five minutes heating at a temperature of 65° C. is sufficient to destroy the activity of this poisonous substance; and, moreover, as was afterwards pointed out by Vaillard and Vincent, that the poison can be separated from a filtered fluid by the method used for separating diastase, that is, along with a precipitate from a solution of calcium hydrate by weak phosphoric acid. This is a very important matter in connection with the production of the toxin of tetanus.

An important fact to be borne in mind is that when this poison is introduced into the subcutaneous tissues it sets up local spasmodic contractions; when injected intravenously general contractions occur at the very outset after the incubation period; the incubation period is, however, well marked in both cases. Now come the observations of Tizzoni and Vaillard, who cut through the nerves of a limb before inoculating the animal with tetanus virus. This limb remained flaccid when all the rest of the muscles had been thrown into a state of spasm. Buschke, adopting a different method, curarised a tetanised frog, and found that tetanus was immediately cut short. It may, therefore, be concluded that the poison does not act directly either on the muscles themselves or on the peripheral nerves. He also found that the tetanic state still remains even after removal of the brain of the frog. Then again tetanus is not set up on the direct application of tetanus virus to the cortex of the cerebrum. On the other hand, progressive destruction of the spinal cord caused the tetanic symptoms to disappear from the part corresponding to the region of the spinal cord removed from the tetanised animal. Consequently the action of the poison seems to be localised in the spinal cord just as in the cases of strychnine and brucin poisoning pointed out by Simpson.

Gumprecht, from a series of experiments on frogs — in one series of which he used strychnine, and in another filtered bouillon cultures of tetanus bacilli — came to the conclusion that the general spasms produced by both substances must be referred to a toxic affection of the central nervous system causing increased reflex excitability of the spinal cord. The local tetanic spasms, although more difficult to explain, he considers also to be due to excitation of the nerve centres, this excitation taking place at a very early period after the introduction of a large dose of the poison, which, as pointed out by Behring and Vaillard and Vincent, may travel in an almost incredibly short space of time from the seat of inoculation throughout the body. Gumprecht maintains, too, that the local spasms around the point of inoculation do not arise reflexly by irritation of the peripheral ends of the sensory nerves; for when the whole of the sensory nerve roots of a limb were cut, and the limb completely anæsthetised, tetanic spasms still made their appearance. He also found that the motor terminal plates and the muscle itself were unaltered by the tetanus poison; as muscles tetanised for a long period still gave perfectly normal contraction curves, and there was complete absence of the reaction of degeneration from such muscles. Gumprecht considers that the local symptoms are most readily explained on the assumption that the poison travels along the nerves, and thus enters the spinal cord at certain definite points, corresponding, of course, to the point of inoculation, where it is more or less localised for some time after its arrival at the cord. In this way he explains the extension of the tetanic symptoms to those muscles which have their nerve-centres in the immediate neighbourhood of those of the nerves which pass from the site of inoculation; it is found also, and probably for the same reason, that the inoculated half of the body of the experimented animal is usually affected earlier and more profoundly than the opposite side.

Goldscheider agrees with Gumprecht that after the subcutaneous injection of the tetanus bacillus, or tetanus poison, the outbreak of general tetanus is preceded by the contraction of those muscles which lie next to the region of inoculation; and he believes that this is due to the action of the tetanus poison on the central nerve cells, in consequence of which they assume an increased and ever increasing excitability, the change taking place gradually, but going on continuously so long as there is an absorption of the poison from the wound. He maintains, too, that the poison is conveyed to the nerve centres by the nerve trunks, and that it there acts on the ganglion cells, increasing their excitability and gradually covering a larger and larger area; but he believes that in addition there is diffusion of the poison by means of the blood and lymph, to which the general spasms are to be attributed. An exceedingly interesting point is noted in connection with the resistance of fowls to the action of strychnine in which irritability of the central nervous system is such a marked feature; for it is found that the fowl has also a similar resistance to the action of the tetanus poison, large doses of which may be introduced subcutaneously with very slight effect indeed. A somewhat similar explanation may be obtained from Brunner's observation, that spasms in the facial muscles are set up both by subcutaneous inoculation in the face, and by subdural inoculation in the opposite half of the brain. Kübler in a note on this observation points out that tetanus in man does not follow the course above described. In man local symptoms in the vicinity of the site of infection are seldom manifested; trismus is as a rule the first sign, the pharyngeal muscles are then affected, and gradually in turn the muscles of the trunk and the lower limbs. This criticism, however, does not appear to be very forcible. In cases of tetanus in the human being, except in those which run their course with exceeding rapidity, the formation and diffusion of the poisonous products of the tetanus bacillus go on much more slowly than in animals under experiment; and it appears quite probable that, as diffusion takes place so slowly, a certain time is required for the poison to accumulate to a degree sufficient to give rise to manifest symptoms of nervous irritation. If this be so, those muscles which are least under control, and which under emotion are most readily stimulated, would be first attacked, and this appears to be the order in which they are attacked in tetanus — those muscles, that is, are first attacked which are least under control of the will, and in which the inhibitory mechanism is least strongly developed.

Following up Pasteur's and Salmon and Smith's experiments on the production of immunity, and on the antitoxic power of the serum of immunised animals in the treatment of a particular specific septicæmia, certain experiments were made on the establishment of immunity from tetanus. For a long time these experiments bore little fruit. At length Behring and Kitasato succeeded in producing a transient immunity in rabbits by inoculating them with the filtrate from a culture of the tetanus bacillus, and then injecting at the same point a small quantity — 3 c.c. of a 1 per cent solution — of terchloride of iodine for five days at intervals of twenty-

four hours. On injecting 0·2 c.c. of the blood of a rabbit so immunised into a mouse (an animal in which they had previously failed to obtain any immunity), the animal was found to have become protected to a certain extent against the disease when the virus was inoculated subcutaneously. This same treatment also proved efficacious when carried out after mice had already been infected with the tetanus bacillus, and even after symptoms had appeared after such infection. It was found, moreover, that as much as three hundred times the lethal dose of a virulent culture, if first mixed with a certain quantity of serum from an immunised animal, might be injected without producing any morbid symptoms. The following year Tizzoni and Cattani confirmed Behring and Kitasato's observations on the specific antitoxic power of blood serum taken from immunised animals. Roux and Vaillard obtained similar results by taking four to five weeks old bouillon cultures of the tetanus bacillus, passing them through a Chamberland filter to keep back the bodies of the bacilli, and then injecting them, mixed with weak iodine solution, using less and less iodine at each successive injection until, as the animals became more and more poison proof, considerable quantities of the unmixed fluids could be tolerated. Once attained, they found that this immunity may be easily kept up by fortnightly injections; but that if the animal be left untreated for a fortnight or three weeks the antitoxic power of the serum begins to diminish, though it may not be entirely lost for a very long time—say a couple of years. When tetanus poison is injected it is absorbed rapidly, and antitoxic substance almost as rapidly makes its appearance in the blood; Roux points out that thirty-five minutes after the injection of toxin into the abdominal cavity of a rabbit antitoxin may be found in the blood drawn from the lateral vein of the ear.

Tetanus was really the first disease of this class in which careful investigation led to results which, though comparatively unimportant in themselves, paved the way for the more important serum treatment of diphtheria. In tetanus there was a certainty of obtaining definite symptoms in animals in which the experimental infection succeeded; here also the toxic products of the bacillus could be readily separated, and the dose required to produce certain symptoms accurately determined. Ehrlich, and Tizzoni and Cattani again, experimenting with the rat and rabbit and treating them with the blood serum of animals which had been rendered refractory to tetanus, maintained that they were always able to obtain a cure if the injections were commenced as soon as the slightest symptoms manifested themselves. When the local symptoms were established, or beginning to disappear, the results obtained by the serum treatment in their hands were slower and less certain; while in those cases in which tetanus was already becoming generalised success never followed this treatment. In the light of the somewhat unsuccessful use of antitoxic serum in tetanus in the human subject, it is interesting to find that the quantity of serum required for a successful result after local symptoms have commenced is at least one

or two thousand times greater than that required to confer an antecedent immunity. This remarkable fact should be borne in mind in determining the efficacy of the antitoxic serum method of treatment. Further, it is calculated that a dose of serum at least 150 times as great as the above must be employed if any success is to be obtained when the local symptoms have reached their height.

The curative action of the serum is said to depend entirely on the proportion of antitoxin which it contains, so that given the proportion of antitoxin in the serum the dose can be accurately calculated. Antitoxin is said by Roux and Vaillard to be an enzyme, which it resembles in many respects, but it differs in its comparative stability; it will stand even a temperature of 70° C. without undergoing any appreciable alteration. Tetanus antitoxin may be kept indefinitely by evaporating blood serum at low temperature in vacuo. At the moment of using it is dissolved in six times its weight of sterilised distilled water.

Tizzoni and Cattani found that the antitoxic substance, when precipitated from the serum by alcohol, does not lose its strength; they urge, therefore, that the alcoholic precipitate, which is non-dialysable, may be substituted for the serum itself. Assuming that the experiments made on the rabbit can be applied to man, they calculate that it would be necessary to give 0·7 c.c. of the serum, or 0·06 gramme of its alcoholic precipitate, at the outbreak of the first symptoms of tetanus; whilst at a more advanced period it might be necessary to inject 210 c.c. of serum, or 12 grammes of its precipitate. This is an exceedingly large quantity to inject subcutaneously, yet in medical practice even this quantity has failed to give satisfactory results. In fact, these observers were unable to obtain a much greater percentage of recoveries by this method than had previously been obtained in cases treated without serum. They were the first to differ from Behring who maintained that the antitoxin, or the antitoxic serum, directly destroys or antagonises the toxin formed by the tetanus bacillus; they rather ascribe to it a power of enabling the tissue cells to continue their work in the presence of larger doses of poison. Roux and Vaillard also maintain that Behring's theory is untenable, namely, that each injection of toxin diminishes the immunising power of serum; and that, if too large or too frequent doses be injected, the antitoxic property of the blood may disappear for a space and the blood actually become toxic. Were the antitoxic serum merely a neutraliser of the toxin, the horse under these conditions should manifest the symptoms of tetanus. This, however, is not the case, and since the antitoxin has disappeared, the immunity of the animal must depend upon something else, a something which appears to be the habituation of the tissue cells to the presence of the toxin; the cells can go on doing their work under the gradually acquired new conditions, and no tetanus is set up. This result is best obtained by the injection (into a horse) of 200 or 300 c.c. of the toxin, after which dose the animal is ready to supply a sufficiently potent serum.

Antitoxic serum confers an immunity which is perfect for a time, but

is more transient than the immunity brought about by the injection of toxins or of the specific organism (when it may last for as long a period as a couple of years). In most cases it is lost at the end of six or eight weeks. Immunity certainly continues as long as any antitoxin remains in the blood. As would be expected, therefore, the antitoxic property of blood disappears long before the immunity of the animal from the disease is lost. This immunity can only be obtained with the toxins when they are injected repeatedly and in large quantities. It must be remembered in this connection that the antitoxic substance is constantly being excreted by the kidneys, by the mammary, and probably by other glands; but a certain quantity undoubtedly remains for some time after the injections have been discontinued. Ehrlich believes that the hereditary transmission of immunity is due to the large quantities of antitoxin excreted in the milk: if this opinion be true the stability of the antitoxic substance is much greater than has generally been supposed. The practical importance of this assertion should not escape observation.

Although the antitoxin is so rapidly excreted by the glands, it has been observed that repeated blood lettings, if they be carried on during a short period, do not seem to lower the antitoxic power of the serum.

In man, as in animals, it is found that the shorter the incubation period — that is, the period intervening between the infection and the outbreak of the disease — the more severe the disease and the worse the prognosis. It is stated that of those cases where the incubation period is under ten days, not more than 3 to 4·5 per cent recover; when the incubation period is from eleven to fifteen days, 25 per cent recover; in those cases in which the incubation period is still longer, about half the patients attacked throw off the disease. Different authors give somewhat different statistics, but these are the general results.

Dr. Kanthack, in a series of tables of the cases that have been treated with antitoxin serum, gives the duration of the incubation period, date of the disease when treatment was begun, quantity of serum injected, the result and the duration of the illness. It is gathered from these tables that the cases of cure all belong to the chronic or benign (?) form of tetanus; whilst those cases that ended fatally were invariably developed in less than fourteen days; in the majority of cases the duration of the disease did not exceed four or five days. In these cases, too, the period of incubation was comparatively brief. These tables have been brought well up to date, and bring out the fact that, so far, the success obtained by the antitoxic serum treatment of tetanus is comparatively slight, except in exceedingly chronic cases, where it appears to have been attended with a little more success than has been attained by the ordinary methods.

Ehrlich's theory of immunity is based upon the fact that in an animal immune from a specific infective or toxic disease the tissues are poison proof; that is, the poison (the tetanus poison, in this instance) can no longer exercise upon the immune animal or its tissues any deleterious effects. As is well known, some animals are less susceptible to the

action of certain specific infective diseases than are others; and in the case of tetanus it has been found that comparatively insusceptible animals — such as the dog and the fowl — may be rendered less and less susceptible, by the injection of gradually increasing doses of the specific poison. It is then found that their serum (although previously it had no antitoxic action when injected into another animal), and in cattle the milk, and in the fowl the yolk of the egg, have, as the result of this treatment, acquired considerable immunising power; and this serum (or these other substances) on being artificially introduced by injection into susceptible animals acts so rapidly upon their tissues that they in turn are rendered comparatively insusceptible. This power, as we have already seen, is extremely well marked if the serum be introduced at the same time or shortly after the tetanus poison; but its power of doing good diminishes more and more rapidly as the tetanus poison obtains a longer start.

Susceptible animals, such as the mouse, rabbit, horse and sheep, may also be immunised; but in their case the process requires to be much more carefully carried on, and is necessarily much more tedious and prolonged. Behring after long-continued experiment found that he was able to obtain the necessary immunity by injecting bouillon cultures of the tetanus bacillus, to which had been added a solution of iodine trichloride, first in the proportion of 0·25 per cent, then of 0·2 per cent, then of 0·15 per cent, until, finally, unaltered culture was used, first in small doses at intervals of three to five days, then in constantly increasing doses at intervals of eight days. In place of this method Vaillard has produced a similar immunity by injecting for a few days a filtrate previously heated to 60° C., then a series heated to 55° C., and finally to 50° C. Gram's solution and lactic acid have both been also used for the purpose of attenuating the strength of the tetanus poison and the activity of the bacilli.

Behring has shown that mice which had been poisoned with fatal doses could be cured even after the appearance of the first tetanus symptoms, in some cases five hours after. The animals survived, but only after a prolonged illness; and if he allowed a period of twelve hours to intervene between the first appearance of the tetanus symptoms and the commencement of treatment, the cases almost invariably had a fatal termination. He worked this out so accurately that he found if the animal were treated before inoculation with the tetanus bacillus it required for its protection only one-hundredth part of the dose that was necessary if the treatment was not commenced until a quarter of an hour after infection.

The immunising serum appears to have a special action on the same tissues as those attacked by the poison — probably on the ganglion cells of the central nervous system; and the substance first in the field, be it toxin or antitoxin, appears to work at a very great advantage over that subsequently introduced. It should be pointed out that even in those cases in which, through the use of large doses of antitoxic serum, the

action of the toxin is brought to a standstill, these cells may, before the treatment commenced, have suffered very considerably; if so the recovery must necessarily be slow: in other cases the damage to the tissues may be so far advanced that recovery is impossible; for it must be borne in mind that the antitoxin can play no part in regenerating structures already destroyed or impaired. Its power appears to be, if used sufficiently early, to fortify the cells against the action of the poison, allowing them to carry on their work unchanged in the presence of what, under ordinary conditions, would lead to their complete disorganisation. It should be noted in this connection, too, that the symptoms of spasm and irritability, for some short time after the exhibition of the dose of serum, are considerably increased; as though a contest for the mastery were actually taking place in the central nerve-cells. The more marked this feature the more prolonged is the process of recovery. It indicates, apparently, considerable disorganisation of the cells before the antitoxic serum has had time to act. German observers agree with Tizzoni and Cattani that, up to the present, no case treated by the antitoxic serum method has recovered which might not have recovered under ordinary treatment; none of them were so acute as to indicate a fatal prognosis. On the other hand this method does not give rise to any unfavourable conditions, so that in cases in which dirty wounds might contain the factors of tetanus, prophylactic doses of the tetanus antitoxin might be injected.

While on this point, it may be well to indicate the difference between the results obtained by the antitoxic serum treatment in tetanus, and by the similar method of treatment in diphtheria. In both cases there is a manufactory of the poison on or near the surface of the body. In both cases there is an absorption of this poison into the body, and in both cases the nervous and muscular systems are specially attacked by the poison. But in the case of diphtheria our attention is called to the manufactory of the poison at a very early stage of the disease; for it usually occurs in some part of the throat, where it gives rise to considerable discomfort: moreover, from the nature of the tissues in this region a false membrane is usually formed at a very early stage of the disease. Attention is therefore drawn to the local poison manufactory almost as soon as it begins to discharge its poisons into the system, and the serum may be utilised to antagonise the poison before it has had time to injure the nerves and muscles. It is interesting to note, too, that in a large number of cases of diphtheria paralysis, the diphtheria has been said to be slight; that is, the local manifestations of the disease have not attracted attention, and the process has been allowed to go on so long that the poison, though perhaps small in amount, has been allowed to act for a considerable length of time, and thus to bring about paralysis. In tetanus, on the other hand, the local wound by which the poison is absorbed is for a long time looked upon merely as a wound, a suppurating one perhaps, but not a manufactory of the tetanus poison; consequently nothing is known of the tetanus until the poison has had time to exert its evil influence on the nervous system:

now by the time we find out that the patient is suffering from tetanus this disease is so far advanced that any chance of treating it successfully by means of antitoxic serum is reduced to a minimum.

GERMAN SIMS WOODHEAD.

Symptoms. — The chief symptom and feature of tetanus is the occurrence, and recurrence at varying intervals, of *spasms* of greater or less severity in the voluntary muscles. These spasms are superadded to a state of persistent tension of the muscles which, however, like the spasms, is commonly relaxed during sleep. They sometimes commence in the neighbourhood of the wound and spread to other parts of the body. It was so in a case of gunshot wound of the thigh, in a case of wound in the perineum by a pitchfork, and in the case of a wound in the face by the lash of a whip, all of which I saw. In another case the spasms in the injured part (the thigh) continued after those in the rest of the body had ceased under the influence of chloroform. In all these the affection was severe, and proved fatal. In inoculated animals the earliest tetanic symptoms commence in the muscles adjacent to the wound, and, later, become general (6). But more commonly in man the tension and spasms are first observed in the neck, giving the sensation of ordinary stiff neck from cold. This is quickly followed by tension and spasms of the muscles of the jaw, causing more or less inability to open the mouth or protrude the tongue, the tip of which is pressed between the teeth in the attempt to show it; and the tongue is often wounded by the sudden closure and snapping together of the teeth. The effort to put out the tongue causes spasm of the facial muscles, giving that peculiar strained expression or grin designated the *risus sardonicus*. Often on asking a patient to show the tongue have I been startled by the unexpected manifestation of this fatal omen in cases of wounds which otherwise seemed to be doing well. Coincident with these early symptoms, or soon after, the front of the abdomen is felt to be firm or hard from contraction of the abdominal muscles. There may also be a sense of oppression or pain about the precordia, penetrating to the spine, which is attributed to tension of the diaphragm; though, it may be observed, the tension and spasm of the muscles in this stage are not commonly attended with pain. Soon the spasms extend to the other muscles of the trunk and to the muscles of the limbs, and, in some instances, are so severe as to cause rupture of their fibres; this event has occurred in the *rectus abdominis* and *psoas magnus*. Indeed, a case is quoted by Curling from Desportes in which both thigh-bones were broken by the force of the contracting muscles, and another in which the second cervical vertebra was dislocated. The spasms usually affect the voluntary muscles in all parts about equally, those of the fingers, however, least; and the pain attendant on them varies. I do not think the pain is generally so severe as commonly stated, and it rarely equals that attendant on common "cramp." In some cases it is sufficient to cause the patient to cry out, but often even boys do not give this or any indication of great suffering; the condition is rather

that of forced and distressful straining, which is often very exhausting. When the spasm ceases the patient is worn out, subsides into quietude, and perhaps into sleep. The pain is chiefly felt along the back; and the dominating power, with perhaps more excited contraction, of the dorsal and lumbar muscles, as compared with the muscles in front of the body, causes some arching of the trunk backwards, to which the term of *opisthotonos* has been given. I have not seen this condition in the marked form occasionally described, nor have I seen the bending in the opposite direction called *emprosthotonos*, nor that to one side called *pleurosthotonos*. The spasms arise spontaneously, sometimes waking the patient from sleep. They may be excited by any slight cause which disturbs the patient, and are often induced by the effort to swallow the viscid saliva which accumulates in the mouth, is pressed out between the lips and is a source of much distress. The muscles of the glottis are not uncommonly affected, causing noisy, difficult inspiration, or stopping of the breathing; and death may thus result. Not unfrequently, when the sufferer has become worn out, a severe spasm, compressing the thorax, suspending respiration, and embarrassing the heart's action, squeezes life out, as it were, and leaves no power to recover it. In acute cases death usually occurs about the third day. In less severe cases life may be prolonged for a fortnight or three weeks, or even more. These prolonged cases afford the best prospect of recovery. On the whole, the disease is most severe and most quickly fatal when it commences soon after the injury, and when the injury is most severe. The brain commonly shows no sign of being affected, the intellect remaining clear to the last, though *delirium* has ensued in a few cases. The pulse is quickened during the seizures, but in the intervals between them the *pulse* and the *respiration* may be natural in rate. The *iris* commonly responds to light, and variations which have been observed in the pupil — contraction or dilatation — were probably due to the drugs administered. The *temperature* varies, and commonly rises during the paroxysms. In a case, lately in Addenbrooke's, in which tetanus followed a wound in the perineum by a pitchfork, the temperature was 99·5° on the third day of the attack (the day of admission), on the fourth day it was 100°, and on the fifth day, during a severe and prolonged spasm which terminated the case, it rose to 106·4°. In a lad, who recovered, the temperature was on several occasions 104°–105°, and at these times the spasms were severe and frequent, and the breathing hurried. A similar remarkable or even greater rise of the thermometer (up to 110°) has been observed in other cases, and the high temperature probably contributed to bring life to an end. The thermometer has also been observed to rise after death. In some instances, however, where death has been preceded by a longer period of exhaustion, a fall of temperature has preceded the fatal event.[1] In the

[1] The rise of temperature may be due to the increased muscular metabolism caused by the continuous and the spasmodic contractions, or to an excitation of the nerve heat-centres. This question is much discussed, and many examples given by Rose. "Ueber Starrkrampf," in the *Handbuch der Chirurgie*, von Pitha und Billroth, 1 Band, 11 Abtheil.

case from a perineal wound just mentioned the catheter was required on the third day, though only seven ounces of *urine* were withdrawn. Subsequently the urine was passed voluntarily, though with pain. The amount of urine varies, in some cases it is more, in some less than normal. It has been found to contain the tetanus toxin in considerable quantity, and injection of the urine into animals has induced fatal tetanus. This passage of toxin with the urine has given rise to the idea that an increase of diuresis might assist in the elimination of the poisonous material from the system; I am not aware, however, that the idea has been carried into practice. The presence of the toxin does not cause any increase in the quantity of urine secreted. The amount of toxin in the urine has been observed to diminish after the injection of antitoxin.

As tetanus is not usually attended with fever, so the blood drawn does not present inflammatory characters. The appetite and digestion are good. The tongue is usually whitish and the perspiration excessive. In most instances there is marked and rapid wasting of the system and diminution of strength. This *wasting and exhaustion*, indeed — this rapid wearing out of the bodily powers — constitutes an important and grave feature in the malady, and one which directly or indirectly leads to the fatal result. It is proportionate to the acuteness of the attack, and seems to depend upon some deleterious influence of the toxic agent acting immediately upon the system. I say this because, though much increased by the recurring spasms, it goes on manifestly when these are mitigated or suspended. The spasms, in truth, are but a peripheral symptom of the disease, though they exert a depressing and exhausting influence upon the body.

The *involuntary muscles* do not appear to participate with those of the voluntary system in the disturbances caused by tetanus. The bowels are commonly inactive, the muscles of the alimentary canal give no indication of spasms, and purgatives act as usual. The bladder and heart are in like manner free. Some observers, as Dr. Parry, attach much importance to the state of the heart, and think it to be the organ which first loses vital power; there seems no sufficient reason for this view. The pulse does but vary with the state of the patient, rising during the paroxysms, falling again when they subside, and becoming weaker as the general strength fails; death ensues from general failure of strength or violent general spasm rather than from any special failure or spasm of the heart.

In a young man, a horse-dealer who lived on the other side of Ely, and was confined to his bed by a rather severe grazed wound of the leg, the first indication of tetanus was a shudder, or general spasm, caused by the removal of an adherent dressing. The affection thus ushered in ran on quickly to a fatal termination.

Many cases of so-called *spontaneous* and *idiopathic tetanus* have been recorded in which no wound or other local lesion could be discovered. I remember such a one in a young man in St. Bartholomew's Hospital under Sir Wm. Lawrence. Aperients were given, and he recovered.

The attack has in many instances been attributed to cold or damp. A healthy-looking man, æt. 54, was admitted into Addenbrooke's Hospital, 11th May 1856, with the usual symptoms of tetanus well marked. They had commenced four days previously, with stiffness in the neck and jaws, after exposure to steam and cold winds in his occupation of boiling bones. There was no apparent local lesion. The spasms were severe and general, and attended with difficulty of breathing, attributed in part to the firm closure of the lips. Still he was able to swallow in the intervals, though with some difficulty. Quinine, beef tea, and wine were given in considerable quantities and frequently. Though thinner and weaker he held on without change for a week. After this he grew worse. He could not sleep, yet morphia seemed to do him harm, causing increase of spasm. Chloral did better and gave some repose. On the 26th he began evidently to improve, and he finally recovered, though it was long before he was free from the stiffness in the back, neck, and jaws.

The affection is said also to have occurred in *cases of contusion*, and in *simple fractures and dislocations*. The following case, of which Mr. Charles Lucas, of Burwell, has kindly sent me the particulars, appears to belong to this class. A stalwart man, æt. 30, received a kick from a horse in the left thigh on 9th March 1883. On the 13th, when first seen by Mr. Lucas, there was a hard, brawny swelling, very tender and painful, in the middle of the outer side of the thigh. No scratch or trace of wound was discoverable there or elsewhere. Fomentations and poultices were applied. In the night of the 24th his back and jaw became stiff, he was unable to open his mouth, and swallowing was difficult. Next day these symptoms had increased, and there were violent, painful spasms, with rigidity of the muscles of the face, neck, back, and abdomen; also pain about the region of the stomach, firm clenching of the jaws and complete inability to swallow, the attempt to do so bringing on severe spasms. A free incision into the swelling of the thigh gave vent to a large quantity of fœtid greenish fluid, which was followed by almost immediate relief to the symptoms. On the following day, 26th, and on the 27th he could swallow gruel, and the stiffness and spasms had nearly subsided. On the 28th there was a complete recurrence of all the tetanic trouble, and a cessation of the discharge from the wound. The symptoms again ceased when the wound was freely reopened, and did not recur. The man completely recovered, though the convalescence was slow.

In this and similar cases it is possible that the tetanic symptoms may be due to reflex irritation of motor centres in the spinal cord by the local disturbance, rather than to any intermediate influence of bacilli or toxins acting through the blood.

It is important to remark, with reference to the possibility of the occurrence of idiopathic tetanus, that the reported cases of this nature have in most instances been milder, and have more frequently recovered than the traumatic cases. Still, if the now prevailing view be correct that the disease is due to the introduction into the wound of certain

special bacteria, there must be some lesion to admit of their entrance. This may be an ulcer in the mouth, the pharynx, the alimentary canal (8), or in some other undetected part. Possibly the proportion of recoveries in the supposed idiopathic cases is attributable to the fact that the undetected local lesion is small in them, and the amount or virulence of the infection less.

Diagnosis. — Tetanus may be distinguished from *hydrophobia* by the persistence of the muscular contraction in the intervals between the spasms, evinced by the closure of the jaws, by the hardness of the abdomen, also by the cause of the wound. In hydrophobia there is commonly more wildness of expression, more movement, more jerking of the limbs, greater apprehension of taking any fluid. Even the mere approach of a drinking cup may throw the sufferer into violent spasms.

There is a variety of tetanus, a sort of modification of trismus, described by German writers as *kopftetanus*, or head-tetanus, the special features of which are that it is caused by some injury to the face, and is attended with paralysis of the side of the face injured. I have seen the following examples of it: — (I.) A man, æt. 35, in the Norwich Hospital in 1837, with a wound in the forehead caused by a fall from a cart, lacerating the occipito-frontalis but not exposing the bone. The symptoms began a week afterwards with stiffness of the neck and jaws, and paralysis of the right side of the face, the mouth being drawn to the left. These were followed by frequent severe spasms of the jaw and body muscles, more especially of the fore part of the body, the man bending forwards and clasping his knees with his hands, this being attended with much suffering and difficulty of breathing. There was no loss of consciousness. He died the day after his admission. The brain presented no morbid appearance. The spinal marrow and the lining membrane of the larynx were rather vascular. (II.) A man, æt. 34, was kicked and wounded about the head and face, 19th December 1858. On the morning of the 27th he could not open his mouth wide. On the following night he was troubled and kept awake by sudden closure of the jaws biting his tongue. This occurred each night and was a source of much pain. On the 4th of January he came into Addenbrooke's Hospital. There was a festering wound on the bridge of the nose and scars on the forehead; also imperfect power of movement of both sides of the face, especially of the right side amounting to facial paralysis; inability to open the mouth and protrude the tongue; tension of abdominal muscles; voice indistinct; when he tried to speak he put his finger into his mouth to prevent the lips, which were drawn to the left, being pressed between the teeth on the right side; difficulty in swallowing, partly owing to the difficulty in deglutition and partly to the fluid being returned between the lips. The introduction of a tube into the pharynx caused severe general spasm; enemata of beef-tea and port wine were therefore given twice daily. The choking and throat spasms caused by accumulation of phlegm in the fauces were much relieved by smoking tobacco. He gradually recovered, and the facial paralysis nearly or quite ceased. (III.) A man, æt. 42, was admitted into

Addenbrooke's 21st March 1891, with a wound under the left eye by a kick from a horse. There was paralysis of that side of the face, with clenching of the jaws, abdominal tension, and laryngeal spasms. These last were so severe and almost asphyxiating during the night that tracheotomy was performed, with great relief. On the 23d he became quiet, but for some days coughing and choking was caused by milk and other fluids passing into the trachea and bronchi, and escaping through the wound in the throat. This gradually ceased and he got well. During the spasms which occurred under chloroform, and subsequently through the night, the back and limbs, as well as the right side of the face, were affected. (IV.) A strong, healthy man, æt. 28, on 4th February 1895, fell on to a heap of dirt, and cut the cheek just below the left eyelid. The wound was cleaned, dressed, and united by sutures at the hospital. On the 6th it was again dressed and was doing fairly well. On the 10th he felt a little stiffness of the jaws. On the 11th the wound was again dressed, but the stiffness of the face did not attract much attention. On the 12th this symptom had increased. On the 13th he was admitted into the hospital. Milk was given, but he became less and less able to swallow it. On the morning of the 16th, when I first saw him, the affection had increased considerably. He was unable to open the mouth or protrude the tongue. The attempt to do so caused severe spasms of the face, neck, and back, inducing a certain amount of opisthotonos, also decided spasm of the front of the neck with blueness of the face. There was no hardness of the abdomen and no spasm of the limbs. Decided paralysis of the left side of the face, the mouth was drawn to the right, the eyelids could not be closed, and the left pupil was dilated. He had been able to swallow very little during the night. The case was evidently urgent. Antitoxin was telegraphed for; but before it arrived or other measures were taken he had a severe spasm, during which he became blue and died evidently from laryngeal stoppage of the breath. On post-mortem examination on the 18th no trace of disease was discovered.

It will be observed that in all these cases, in addition to the wound of the face with paralysis, clenching of the jaws, and tension of the abdominal muscles, there was spasm or paralysis of the glottis which constituted the most urgent symptom. This was fatal in No. IV., probably also in No. I., and required tracheotomy in No. III.; in No. II. the pipe of tobacco seemed to give relief. The paralysis of the glottis permitting fluids to pass from the mouth into the respiratory passages was a very troublesome feature in No. III.; and in No. IV. the pupil was dilated. In I., II., and III. the muscular affection did not extend beyond the abdomen, where it caused firmness of the abdominal wall; but in No. IV. the back muscles were affected, and the abdomen was soft. In all the limbs were free. The facial paralysis is difficult to explain. It has been attributed to swelling or some inflammatory or other influence radiating from the wound and involving the facial nerve, to inflammation of the nerve in its course through the temporal bone or on the cranial

side of that bone, but no satisfactory conclusion has been arrived at. In No. IV. the paralysis extended to the iris. There was no loss of consciousness or of sensation in the parts affected in any of the cases.

Rose, in the article before mentioned, gives two similar cases, in one of them the affection extended to the limbs and the patient died; in the other recovery took place. In the early part of last year a case of kopf-tetanus was related by Caretti. There was a lacerated, contused wound of the forehead, paralysis of the face on both sides, and trismus. The arrest of the malady was attributed to the use of antitoxin. Another case in which the cure was also attributed to antitoxin is there quoted. [See also 22.]

The spasms of *strychnia* poisoning somewhat resemble those of tetanus; but they are more sudden and more rapid in sequence, affecting the whole frame, including the digits. The muscular relaxation in the intervals of the spasms is more complete. The affection is more quickly fatal, or on the other hand subsides; a speedy termination which contrasts with the somewhat slower course of tetanus, especially of those cases of tetanus in which there is no discoverable external lesion. Strychnia may be found in the urine.

Tetany, so-called from its simulating tetanus, is a spasmodic affection resulting from an irritated condition of the nervous centres, either originating there, or transmitted from some disorder of other parts, such as the stomach or bowels, the uterus, the urinary or genital organs. It appears to be less common in this country than in other regions. The spasms progress less steadily and recur less regularly than those of tetanus, and they are attended with less wear of the system. Often they are localised, and not unfrequently they are confined to the hands and feet; this is particularly the case in children, in whom the malady, often associated with rickets, easily yields to treatment, or subsides spontaneously. In some instances the spasms are more general, more severe, or more frequent, and they may lead even to a fatal termination. This has occurred in several cases after complete removal of the thyroid gland, and under these circumstances the diagnosis from tetanus might be difficult. One cause of tetany, at any rate, appears to be a deficiency in the secretion of the thyroid gland; and cases of its cure, either after removal of the gland or otherwise, by administration of the thyroid extract, were published last year by Dr. Byrom Bramwell (23). If this sequence be verified thyroid extract would serve as a ready means of diagnosis. Sudden and fatal attacks of tetany sometimes occur in cases of dilatation of the stomach.

The following case, which I saw in consultation with Dr. Buckenham and Dr. Lawrence Humphry, the latter of whom has kindly given me the notes, may be regarded as an example of the severe form of tetany.

A pale, thin, anxious looking lad, æt. 13, sitting on a sofa with the head bent on to the chest, and rigidly fixed in that position; knees firmly extended, and rectus abdominis contracted, mapped into squares, and bending the body forward; upper limbs stiff, but not so fixed

as the lower; muscles of back rigid, and sterno-mastoid and trapezius especially so; muscles of face not rigid; he could open his mouth and put out his tongue, which was much scarred; tenderness over fourth and fifth cervical vertebræ, which were rendered prominent by the bending of the neck; temperature 100°, pulse 90. Slight spasms during the day were easily brought on by movement, swallowing, or any irritation. At night these were severe, causing him to bite his tongue and cry out, and his respiration was then difficult; no loss of consciousness during the spasms, or at other times, and no fits. The affection began three weeks previously without apparent cause, with spasms of the jaw causing him to bite his tongue. The spasms extended and increased in severity. They continued in spite of various treatment, and he died in a month (seven weeks from the commencement of the attack) of exhaustion. A post-mortem examination could not be obtained. It was stated that he had a similar attack, not so severe, three years before, and recovered.

Among the many features which *hysteria* and *hystero-epilepsy* occasionally assume are spasmodic or convulsive seizures; these may present some resemblance to tetanus, but can scarcely be mistaken for it. The sex, appearance, general character of the patient's constitution, and the character of the seizures, are commonly sufficient to indicate the nature of the malady. The writhing, the distortion of features, the laughing or crying, the hallucinations, the more or less complete anæsthesia or paralysis of parts of the body, the affections of consciousness, most of which are due to influences acting on the cerebral hemispheres, are very unlike the manifestations of spinal excitement which we witness in tetanus.

Treatment. — With regard to the treatment of tetanus it is necessary to bear in mind, *firstly*, that, like most other diseases caused by toxic agencies in the blood, it runs a definite course, having, as it were, a certain life-history — a period of incubation which varies from a few hours to several weeks, a period of increase, and a period of decline. These may not be defined or regular as to their time of occurrence or duration, but they clearly exist; and the severity and impression of the attack upon the system may be taken as proportionate to the amount and virulence of the admitted poison as compared with the resisting powers of the individual. *Secondly*, as already mentioned, the symptoms of tetanus are usually seen first in the muscles of the neck, jaws, and face. This early condition has been called trismus; and if the affection go no further the patient commonly recovers. *Thirdly*, we have hitherto, that is to say till recently, known of no antidote or agency whereby the poison could be neutralised or its influence upon the system mitigated. *Fourthly*, our means of modifying the poison being very small, the contest lies between the strength of the attacking poison and the resisting strength of the tissues; and the treatment resolves itself mainly into the adoption of measures which may increase the latter and enable the patient to hold on till the malady runs its course and terminates by resolution. The alleviation of particular symptoms, such as the spasms, may do something to alleviate the distress, but little

to modify the progress of the malady; and the drugs employed for the purpose have often done, on the whole, more harm than good. The only hopeful means of treatment has hitherto consisted in the endeavour to maintain the strength by the administration of nutriment — this being especially indicated by the wasting and exhausting influence which, as already mentioned, forms so prominent a feature of the disease. Unfortunately, in most of the severe cases this cannot be efficiently carried out owing to the difficulty of swallowing; and the difficulty of giving enemata is often such that they cannot be continued, though in some cases they are well borne and should then be persevered with. When food cannot be swallowed recovery rarely takes place, and nothing can be relied on even to postpone the fatal event. A great variety of drugs, chiefly of the sedative kind, have been tried; some have been thought, in particular cases, to have done good, but no decidedly good results have been obtained. Even the relief from distress which may be produced by them does not seem in the severe cases to influence the progress of the malady materially, and the mild cases in which they have seemed beneficial would probably have recovered without them. Electricity, antipyrin, and cold baths have been used, as well as injections of carbolic acid, phenol, and corrosive sublimate; but the cases in which benefit is reported have been of the mild type. In short, whenever the patient can be induced to swallow, the administration of nutriment should be regarded as the sheet anchor, and no medicinal treatment should be allowed to interfere with it. Unhappily, even in these milder cases it will often fail, but, saving the antitoxin method, we have no hopeful resource. The worst case in which I ever saw recovery was that of an infant from whom I had removed a large adipose or fibro-adipose tumour situated in the back of the neck. The spasms were frequent and so severe that, on several occasions, we thought the child was dead. She continued, however, in the intervals to swallow milk. I did not allow any medicine to be given, but relied exclusively upon the milk. Gradually the spasms became weaker and less frequent, the malady ran its course, and the child recovered. I once went several miles to see a case of tetanus in a man, employed in the stables of a horsedealer, who had been accidentally shot in the back of the thigh by his master. I directed the administration of port wine, beef-tea, and eggs, as much as he could take, and prohibited all medicine. It was rather a severe case, but the man got well. I have had other cases treated in the same manner and with the like result. All, be it remarked, were able to swallow, though some with difficulty, and were therefore of the milder type. It is surprising how much nourishment can be taken and well borne in these cases, which indicates that there is no failure in the digestive and assimilative powers.

In the earlier years of my practice I tried a variety of drugs very perseveringly, but without any appreciably good effect. In some instances I thought they had done harm; and I came to the conclusion, after many struggles with the disease, that I could not boast of any success even in prolonging life by these means. Most if not all of

these drugs—such as morphia, aconite, Indian hemp, chloroform, chloral—were given with the view of lessening the spasms which, after all, as I have just said, are but a symptom of the disease; and I found, in some instances, that when the spasms had been delayed they recurred after the interval with the greater severity. In one case, where the wound was in the thigh, I kept the patient continuously under the influence of chloroform for several hours. Then a violent spasm occurred and was fatal. In another case, that of a young gentleman who had received the charge of a gun in the buttock, and in whom the spasms were frequent and severe, at the request of himself and his friends, whom I warned that it would do no good, I kept up the influence of chloroform; and though the spasms were in great measure controlled by it, I thought that it rather shortened life. In yet another case a severe and nearly fatal spasm was induced by the administration of chloroform before amputation of the damaged leg. After the operation and the chloroform there was a temporary cessation of spasm, but the disease ran a fatal course. I may observe that the effect of chloroform varied much in different cases: in some, as in the case just mentioned, its administration caused violent spasms; in others these did not occur. In some its administration was followed by a period of quietude and relief from all distress; in others the spasms seemed to be rather aggravated, and the patient was weaker, as though the chloroform left him more susceptible and less able to bear the attacks. I had some hope from tobacco given in the form of an enema; but it had to be used with much caution on account of its great depressing effect, and after several trials I was not convinced that it afforded any sufficient compensating advantage. One man smoked incessantly and got well, but it was not a severe case; in others the smoking did no good. Nicotine also proved of no avail. In so far as these sedatives have any initial action of stimulation of the ganglionic and other nerves they may indeed do harm. Chloral gives some relief and sleep, and perhaps enables the patient to swallow. In the case of the chronic ulcer of the leg I have mentioned—a woman æt. 50—the dyspnœa from closure of the glottis during the spasms was so urgent that I performed tracheotomy. It relieved that symptom, and the spasms, for a time, were less severe; but she became weaker, and died on the twenty-second day from the commencement of the attack. Opium and Indian hemp in large doses did no real good; and the same, on the whole, has been the experience of others. The extract of Indian hemp, in one case that I saw, was found after death to have accumulated into a dangerous mass in the stomach, where it had not been digested or absorbed. I came, therefore, long ago, to the conclusion that the administration of nutriment was the only hopeful treatment; that where this could be done nothing should be allowed to interfere with it, and that where it could not be done it mattered little what measures were adopted, the result being almost invariably fatal. It need scarcely be added that the patient should be kept quiet and protected from cold, and from all draughts and other external irritants.

The wound should be cleansed from all foreign substances, and freely soaked with antiseptic solutions. Removal of the limb by amputation, also division or stretching of the nerves connected with the wounded part, have been resorted to, but rarely with good result. The poison has already entered the system, and is working its evil way there; and as in the case of hydrophobia, and of primary syphilitic sores when the glands are affected, the further progress of the malady does not appear to be much influenced by the removal of the primary source of infection. Where a good result has followed, the same would probably have ensued had there been no surgical interference. Thus, in a lad æt. 13, admitted into Addenbrooke's a fortnight after a contused wound of the fourth and fifth fingers, the fourth finger, which was in a foul state, was amputated under chloroform, a bad spasm occurring when he was being anæsthetised. The spasms were not very severe, the temperature never rose above 100°, and he took nourishment. Chloral hydrate and bromide of potassium were given; the spasms diminished in frequency and severity till April 16th, when the last occurred, and he got quite well. Gross (i. 633) relates that in a case of tetanus he dissected out from the face of a girl a tender cicatrix which had followed a lesion from a splinter of wood a month before the occurrence of tetanic symptoms; no further paroxysms occurred. On the other hand I have seen amputation of the leg in four cases in which tetanus ensued upon injuries to the foot, but without good effect in any. A more favourable view of the operation seems to be afforded by the *Surgical History of the War of the Rebellion* in America (*vide* Appendix), where it is stated that the operation was resorted to in twenty-nine cases after incipient tetanic symptoms, with favourable results in ten. It is not stated whether in these cases the disease was acute or chronic, though it would appear to have been acute in four out of the seven cases related. The observation that the bacillus germinates chiefly in the deeper parts of the wound, and disseminates itself in the surrounding tissues, renders free excision or amputation necessary if any local measure of this sort is attempted; and of no less importance for the prevention of tetanus is the free cleansing of the wound with antiseptic solutions in all cases if, as appears to be the fact, the bacilli have their seat and residence in and near the wound, where they generate the toxin which enters the blood, and if their development and increase are favoured by the presence of pus.

If by extraction of one or more teeth, or by the nostril, no way can be made for the passage of a tube, the operation of *gastrostomy* has been rendered comparatively so safe and simple by the modern appliances of surgery, that it might be resorted to in some of those cases of medium severity in which swallowing is difficult or cannot be accomplished. The requisite steps should be taken to open the stomach at once and introduce a tube through which nourishment may be passed with a free hand. I am not aware that this proceeding has been tried or even suggested; but I think it deserves consideration, and it might prove an

assistant to the *treatment with antitoxin* by maintaining the strength during the days in which that remedy is being employed.

For a new hope is dawning with regard to the treatment of this and of other affections, dependent like it upon a toxic infection of the blood; a hope based upon a method which is really antidotal, and consists in the introduction into the system of a material engendered by the poison or toxin, and called antitoxin. Should this hope be realised in the future application of the method, one which concerns not tetanus only but other kindred diseases also, we shall be able to boast of the most important discovery ever made in therapeutics, one of the most important ever made in medicine — perhaps the greatest and most beneficent medical discovery of our generation. In what manner the antitoxin is produced, whether by the toxin stimulating the cells or other tissues of the body to its formation, or by any change, such as an increased oxygenation, which the toxin itself undergoes, or from the disintegrating bodies of exhausted or dead bacteria, or by what other process, is not clearly known. It seems to act, like the toxin, as a ferment. Thus we have in the blood, at the same time, the two ferments — the poison and its antidote, the toxin and the antitoxin — the one leading to the production of the other; and also, somewhere within the surface, the bacteria which are the source of one or the other, of the poison and its antidote, or of both. In the case of diphtheria this therapeutic method is so far gradually gaining ground. In tetanus it has not been tried in a sufficient number of severe cases to enable us even to come to a provisional conclusion; and some at least of the milder cases might have recovered equally well without it. The general opinion, however, seems to be that in many of the cases in which it has been tried it has so far afforded relief as to justify the hope that further experience will show, at any rate, that it has more potency in resisting and overcoming the malady than any other agent which has yet been tried (9). We read that in several cases of the milder kind where it has been tried the spasms have been mitigated, and the amount of toxin in the urine has been reduced; there seems to be no record of any acute case in which the antitoxin treatment was even of temporary benefit. It has been noted also that the symptoms have returned during the temporary suspension of the injections, to be mitigated again on their resumption. We read, too, that a large proportion of the recorded cases in which it has been used have recovered, though, as I have already said, these were chiefly of the milder type (10); it does not seem to have been productive of ill effects in any of the cases. In most cases the relief afforded by the antitoxin injections, if any, was soon manifested. In some there was a longer interval, the symptoms continuing unabated or even increasing at first, though they ultimately yielded to the influence. In two cases of "kopftetanus" referred to above the good results were attributed to the use of antitoxin. These and other variations in the effects of the agent may not improbably have depended on variations in its strength and quality or on the method of its preparation. Respecting

all this there is much to be learned, and we must look for practical information concerning the antitoxin treatment of tetanus, in the main, to those countries in which the disease is more frequent than happily it is in our temperate regions. In our own country the cases are comparatively few and sporadic, and they occur without any warning; there is nothing in the nature of the local lesion to give intimation of the probability of so serious a complication. Hence the practitioner is probably not at once prepared with the means of giving trial to the antitoxin treatment. Happily the remedy is becoming less expensive and more easily procurable in an emergency. It may now be obtained from Messrs. Allen and Hanbury, in Plough Court, E.C., at a moderate cost, though as many as thirty injections or more may be required in the treatment of a single case. It must be used early; the cases, therefore, in which it can be tried with good hope of success are few, and some time must elapse before we can form a true estimate of its value. We should, at any rate, whether we resort to the new remedy or not, persist in the plan of treatment which I have indicated, and maintain the strength of the patient till the storm is overpast, in the hope that the vessel may be enabled to weather its blasts.

When the disease subsides the spasms become less severe and less frequent, the face more natural, and the periods of sleep longer and less disturbed. For a considerable time after all spasms have subsided a sense of stiffness, as if from cold or rheumatism, is experienced in various parts; it is longest felt in the neck, back, and loins, and is liable to be increased by exposure to damp or cold, or by fatigue. It is in some cases felt about the jaws for months. Much care in diet and in the avoidance of cold should be enjoined, for instances have occurred in which the disease has returned after many days somewhat in the manner of relapsing fever.

Morbid Anatomy. — The examination post-mortem in cases of tetanus has commonly revealed to the naked eye no trace of disease in any part of the body. Naturally, attention has been directed chiefly to the nervous system; but here, for the most part, whether in the brain, spinal cord, meninges, or nerves, nothing abnormal has been discovered. In a few cases, it is true, congestion has been observed in the spinal cord, or in its membranes, or in both, more particularly about the regions connected with the nerves of the injured part. This congestion has, in some instances, been attended with changes or degenerated conditions in the gray matter of the cord, and some swelling. Thus an instance is related by Dr. Dickinson (11), in which there was, in addition to the congestion of the dura mater and the pia mater, swelling of the cervical and lumbar portions of the cord caused by transparent exudation into the substance of the cord with consequent lesion of the substance. Lockhart Clarke and Clifford Allbutt also found swelling and areas of disintegration of the gray matter of the cord with exudation of finely granular matter and débris of blood and vessels. The nerves in the neighbourhood of the wound have also been found inflamed. These occasional appearances

confirm the view, which on other grounds can scarcely be doubted, that the tetanus poison vents itself in an especial manner upon the spinal cord, causing functional disturbance; though it is usually attended with little or no gross structural lesion. This absence of actual nerve lesion formed an argument (12) against the supposition that the real, at any rate the primary seat of the disease was in the nervous system itself, and prepared us for or suggested the view, since confirmed by the bacteriological investigations, that blood-poisoning by noxious material introduced into the system must be the essential cause of the malady.

The *rigor mortis* is said to persist long (13). As already stated, certain muscles have been found ruptured, and even bones broken, by the force of the spasmodic contraction of the muscles.

Infantile Tetanus (*Tetanus neonatorum*)

Is commonly, and probably with reason, attributed to some infection taking place at the umbilicus. I have only seen one case: the child was stiff all over, persistently so, as far as I could judge, and did not live long. Escherich (14) has tried the antitoxin treatment in four of these cases, of which one recovered. In case 1 the doses administered were too small in quantity; in case 4 the disease was exceptionally severe, so that a good result could not be expected; in case 3 the injections had to be discontinued in consequence of the onset of septic pneumonia. Inoculation of mice from two of the cases (1 and 4) with a bit of tissue taken from near the umbilicus caused typical tetanus; but in the other cases the inoculation was without result. The disease is said to be common in some regions, especially in India, where antitoxin has been tried, at least in one case, but with no good result (15).

APPENDIX

History of War of Rebellion. — The fullest statistical record hitherto published is to be found in that marvellous compilation and evidence of American work, the *Medical and Surgical History of the War of the Rebellion*, third surgical vol. p. 818. Of 246,712 injuries by weapons of war 505 (0·20) per cent, or a little over 2 in 1000, were followed by tetanus, which is regarded as not a large proportion. The seat of the injury and the result are tabulated as follows: —

Seat of Injury.	Total Cases.	Recoveries.	Deaths.	Ratio of Mortality.
Head, face, neck	21	1	20	95·2
Trunk	55	5	50	90·9
Upper extremity	137	18	119	86·8
Lower extremity	292	30	252	89·7
Aggregate	505	54	451	89·3

"The belief that wounds of the foot and hand are particularly liable to cause tetanus is not confirmed by the cases recorded during the war." The

rarity of tetanic complication of chest-wounds is noted; and in all but one of the 17 of these there were injuries to scapula, shoulder, or arm.

In 131 instances tetanus followed closely upon operations in the extremities, namely, in 116 cases after amputations, and in 15 after excision.

The recoveries were chiefly in the slighter or more chronic cases; and the later the occurrence of the disease after the injury the greater the chance of life.

In 6 cases the disease occurred within twenty-four hours after the injury. Few on the second, third, and fourth days. From the fifth day the number rapidly increased until the eighth, when it diminished till the fourteenth day; after which it "appeared irregularly" — in one not till seven months after the injury.

In 203, one more than one-half, the duration of the disease did not exceed three days; of these only two recovered. The longest duration of the fatal cases was twenty-seven days.

In several instances the removal of the missiles or foreign bodies, or pieces of bone, seemed to have quieted the threatening symptoms.

Amputation was resorted to in 29 instances after incipient tetanic symptoms; 10 of the cases resulted favourably. This is very strong evidence in favour of the proceeding; but it is not stated whether the disease was acute or chronic. In 4 of the seven cases related it would appear to have been acute. Relief was afforded by the chloroform and continued after the operation. No anatomical lesions of the medulla oblongata cerebellum or spinal cord were found in the cases that were examined post-mortem.

GEORGE MURRAY HUMPHRY.

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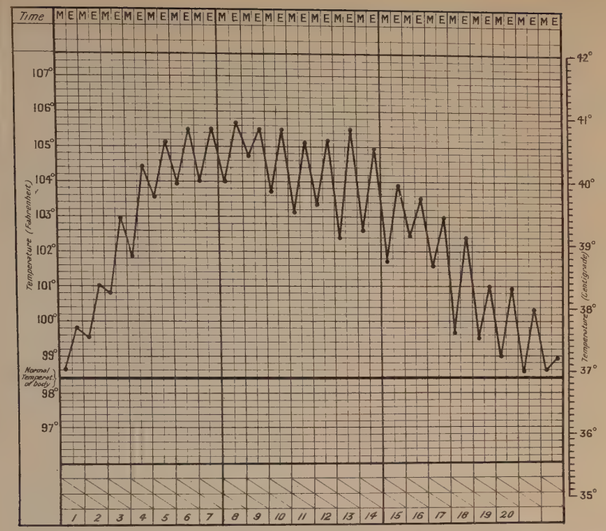
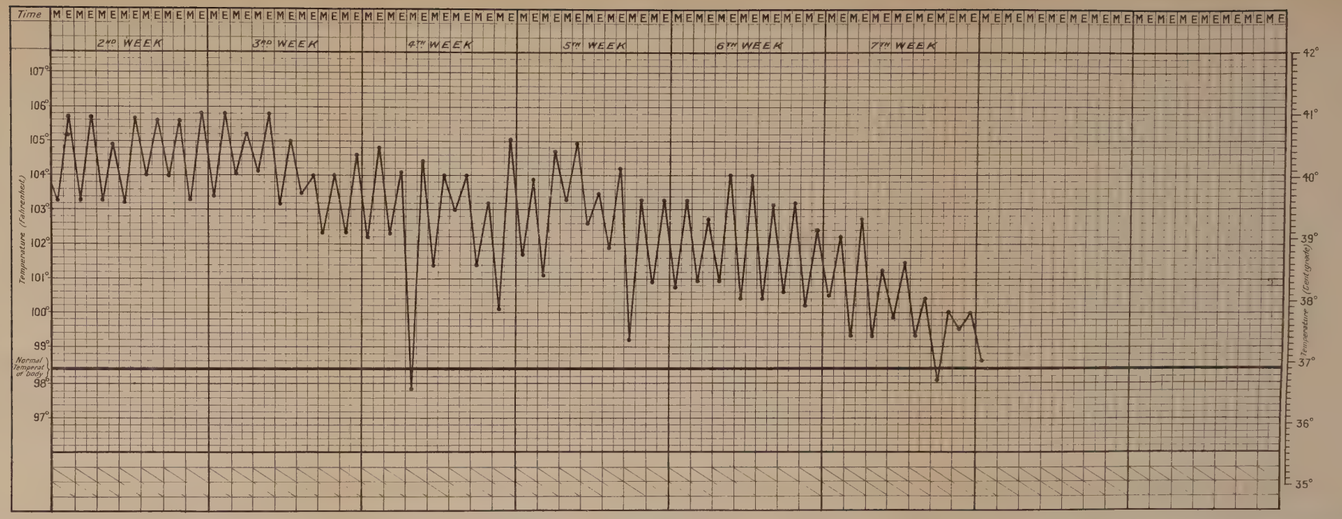

Time
Temperature (Fahrenheit)
Temperature (Centigrade)
Normal Temperature of body
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20



DISEASE.

Enteric Fever with 3 relapses.

Notes of Case.

Name { Jane B——

Age – 17

Diet

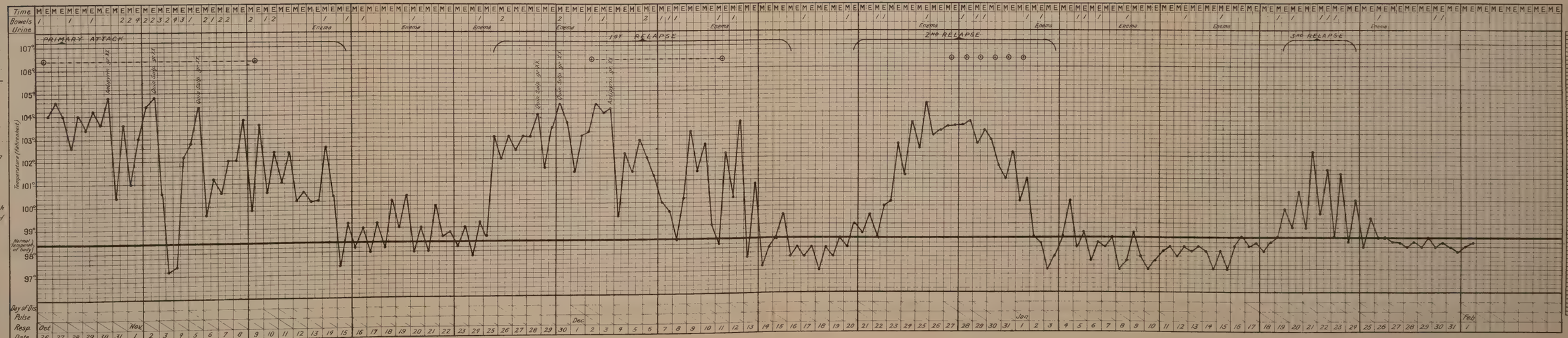
Case Book N°

Reported by D^r A Johnson Med Chronicle (Vol XIV. p 102).

o------o Indicates dates on which rose spots were noticed

Date of admission Oct 26 1890

Result – Recovery.



Dreschfeld's Enteric Fever

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ENTERIC FEVER

Synonyms. — Gastric Fever, Typhoid Fever, Pythogenic Fever; Fr. *Dothién entérite, Fièvre typhoide;* Germ. *Abdominaltyphus, Nervenfiebre.*

Definition. — An acute infectious fever, due to a specific micro-organism, occurring endemically, sometimes epidemically; *clinically* characterised in ordinary cases by a gradual onset, followed by a period of continuous fever with diarrhœa, an enlarged spleen, tympanites, and a roseolar rash, usually lasting three weeks; *anatomically* characterised by more or less extensive ulcerations affecting the Peyer's patches in the ileum, with swelling of the mesenteric glands and enlargement of the spleen.

History. — Enteric fever appears to have been known to the ancient writers (for example, Hippocrates and Galen); but it was not until the beginning of this century that it was distinguished from other acute febrile affections, especially from typhus.

In Germany Von Hildsbrandt (1810) clearly distinguished these two affections; in France Bretonneau (1818) proposed the name of dothiénentérite, to denote the specific nature of its intestinal lesion; whilst in England, after some older writers, the observations of Perry (1836), Barlow (1840), Stewart (1840), and especially the classical papers published by Sir Wm. Jenner (1849–53), led to the final distinction between the two diseases, which ever since has been universally recognised. Enteric fever having then been recognised as a specific fever, its etiology was made the subject of further investigation. Its infectious nature, and its propagation by the fæcal discharges of the patient, led many physicians, headed by Budd, to look upon it as due to one specific agent, and to deny its origin *de novo.*

The advances made in sanitary science, the establishment of special sanitary medical officers, and the interest with which all matters relating to public health were considered by corporate bodies, a movement in which England took a prominent part, led on to investigations into the

cause or causes of enteric fever; and though the agent was not discovered, yet the source of the propagation and dissemination of outbreaks were carefully studied, and many of them were traced to contaminated water or milk and to "sewer gas." This led to the improvements in drainage and water-supply of many English towns, with the result of a marked diminution in the prevalence of enteric fever, and of an almost total extinction of typhus (see Table I., Appendix). With the development of bacteriology the history of typhoid fever entered upon a new stage.

Murchison, whose classical writings on the continued fevers of England still maintain a prominent place in the literature of enteric fever, believed in the origin of enteric fever from decomposing organic material, and also in its spontaneous origin. The observations of Stich and later of Panum, which showed that the ingestion of putrid material may produce, amongst other symptoms, fever, diarrhœa, and intestinal lesions, not only supported this opinion, but gave rise to that of the autogenetic origin of enteric fever, namely, that the disease may be generated in the system from decomposition of fæces in the intestinal canal without any infection from outside.

Eberth (1880) discovered a peculiar bacillus in the organs of persons who had died of enteric fever, and subsequent investigations not only confirmed this observer, but placed the pathogenetic nature of this organism, and with it the etiology of enteric fever, on a firm basis; thus the pythogenetic theory of Murchison and the autogenetic theory of other observers became untenable. The discovery, however, of another micro-organism — the bacterium coli commune — which occurs in the normal human body, and apparently elsewhere also, which is seen in increased numbers in persons affected with enteric fever, and in many of its characters and properties resembles the bacillus of typhoid fever, has led authors to review the older theories: some, like Roux and Rodet, believe that the bacterium coli commune may be converted, under suitable circumstances, into the typhoid bacillus; others, like Peter (68), hold that in typhoid fever we have simply an intoxication of the human body by the retention of substances elaborated by it. The majority of pathologists and clinicians, however, firmly believe in the specific nature of enteric fever, as thus only is its infectious nature explained — though, on the other hand, the mode and source of infection in many cases are difficult to prove.

In sketching the history of enteric fever the progress in the treatment of the disease must not be forgotten. Whilst depletion and starvation were for a long time the guiding principles in the treatment of fever, the liberal use of stimulants was advocated chiefly by English physicians (Alison, Graves, Todd, and Stokes); but in the course of time their administration was again restricted, and used only on definite indications. The antipyretic treatment by the cold bath, however, first recommended by Currie (1787) and resuscitated by Brandt (1861), is said to have diminished considerably the mortality from enteric fever, and is now widely adopted. The various antipyretic drugs and their

application in febrile diseases have scarcely displaced the cold water treatment. With the discovery of the typhoid bacillus new methods of treatment have been tried: the antiseptic treatment proposed by Bouchard (though antiseptic drugs had been given long before in enteric fever), and subsequently adopted in various forms by many English and continental observers; and more recently a quasi-specific treatment, consisting in the subcutaneous injection of sterilised cultures of typhoid bacilli have been tried, but the latter method is yet in the experimental stage.

Geographical Distribution. — Enteric fever prevails all over the globe. It is endemic in Great Britain, but is less common in Scotland than in England or Ireland; its frequency in the British Islands has, however, considerably diminished during the last ten to fifteen years, owing to better sanitary arrangements. It is met with throughout the whole of Europe; it is widely distributed throughout the whole of the United States and Canada; it is met with in India, Africa (Egypt, Tunis), and in Central and South America.

Etiology. — The *specific* cause of enteric fever is the *bacillus of typhoid*, or *Eberth's bacillus*. This organism was first described by Eberth (22), who found it in sections of the mesenteric glands and of the spleen of persons who had died of enteric fever. Koch about the same time gave photographs of the same organisms present in the tissues, and Coats of Glasgow also described and figured them. Gaffky prepared pure cultivations of the bacillus, and described some of its chief morphological properties. Since then numerous observations have been made on the morphology, life history, distinctive characters, and pathogenetic nature of this organism; the more important of these features will be described in the following account, in the working out of which I have been greatly assisted by Mr. James Richmond, who for many months has studied the bacteriology of enteric fever in the pathological laboratory of the Owens College, and has tested the statements of other observers by his own investigations.

Character and Biology of the Typhoid Bacillus. — The appearance of the bacillus may be studied from sections, from juices and scrapings of the organs, and from pure cultures.

The typhoid bacillus may be seen *in sections* prepared in the usual way, stained for twenty-four hours in Loeffler's alkaline methylene blue solution, or in Ziehl's carbolic fuchsin, and washed subsequently in water so as to wash the dye, if possible, from all that appears in the sections except from the bacteria and the tissue nuclei; they are then dehydrated in aniline oil: if now washed in alcohol, or treated by Gram's method, the colour is removed from the bacteria, but if the section be placed for ten minutes in a one-fifth per cent solution of mercury dichloride, and then stained by Gram's method, the bacilli take the stain deeply [Woodhead]. In preparations made from *the juices* of the organs or *from cultures* on cover-glasses, watery solutions of any of the aniline dyes, especially fuchsin or Ziehl's carbolic fuchsin, may be used as stains; in the latter case a much shorter action of the stain is necessary. The cover-glass is rinsed in water, dried, and mounted in xylol balsam. Washing with

alcohol or the use of Gram's method removes the stain entirely. They often stain at the ends, leaving, with the watery dyes, a bright unstained portion in the centre.

The typhoid bacillus is a short, thickish bacillus — 2–3 μ long, and 0·7–0·9 μ in breadth — having rounded ends; cultivations outside the body often grow in threads composed of bacilli strung end to end; in sections the bacilli are single. In drop cultivations they have very lively motions of progression; the longer threads have a slower sinuous motion. When stained by Loeffler's method (60), or one of its modifications, they are seen to be provided with a number of (8–12) fine wavy flagella having a length twice that of the bacillus. These are inserted at the sides as well as into the ends of the bacillus.

The bacillus grows in the ordinary nutritive media. Its growth is favoured by the presence of oxygen and a temperature of 25°–35°, although growth can go on in the absence of oxygen (Liborius and Roux) and at lower temperatures.

In plate cultures, on nutrient gelatine, the youngest colonies seen under a low power are round or oval, and of a yellowish colour and sharp outline. The older, deeper colonies are darker, with regular borders and fine irregular linear markings. The superficial colonies grow quickly into an expansion, which may attain to a diameter of 3–4 mm., having a notched border, a grayish white colour, and a furrowed and wrinkled iridescent surface. The gelatine is not liquefied.

Gelatine stab cultures show the same appearance of the superficial and deep growths.

On agar there is a superficial white growth.

On solidified blood serum a white superficial growth occurs, without liquefaction of the serum.

On *ordinary potato* the growth is scarcely to be distinguished in forty-eight hours, only a moist appearance being noticeable. The area of inoculation when touched with the platinum needle has a feeling of greater resistance than the uninoculated part, and typhoid bacilli are found in the part which offers this resistance to the needle.

On *alkalised potato* older cultures have a dirty yellow appearance, and cultures of typhoid recently isolated from fæces give a thicker, more pulpy growth. The other characters are given in tabular form below.

The bright unstained parts, once supposed to be spores, are known now to be due to retraction of the protoplasm to the poles of the cells where it takes on the stain. This retraction is a sign of degeneration, due to unsuitability of the medium, either from exhaustion of the nutriment, or from an unsuitable reaction (acidity). So far from these forms being spores they are on the contrary more easily killed by heat, drying, and bactericidal substances than bacilli which stain uniformly.

Vitality of Typhoid Bacilli — Influence of Temperature.— The bacilli are killed when exposed to temperatures of 60° C. for twenty minutes (Pfuhl), but in this respect the various cultures show a somewhat different behaviour; low temperatures do not readily destroy the vitality of the

bacillus, and several observers (Chantemesse, Widal, Janowsky, Prudden) have seen cultures of bacilli in beef-tea live for weeks, although repeatedly exposed to a freezing temperature.

By cultivation it has been found that in sterilised stools and in stools which have stood for some time the bacilli may remain alive for months; in fresh typhoid stools and in normal stools they die much sooner. In threads soaked in cultures they remained alive one year; on potato cultures two years; in sterilised garden soil twenty-one days; on sterilised linen sixty to seventy days; in street sweepings thirty days. When *dried* in various ways by more or less active agents their duration of life was from one to sixty-four days; free access of air shortens the duration. *Hydrochloric acid* of the strength in which it occurs in the normal gastric juice does not destroy their vitality till it has been in contact with the cultures for several hours.

Action of Antiseptics. — Seitz found that quinine, chlorate of potash, salicylic acid, and calomel destroyed the life of the typhoid bacilli. Dr. A. C. Latham experimented with calomel, chalk and mercury, β naphthol and bismuth, and found that all, except bismuth, killed the typhoid bacillus.

Carbolic acid (2–3 per cent solution), and corrosive sublimate (1 in 5000) also quickly destroy the typhoid bacilli. From a prophylactic point of view the observations of Liborius, confirmed by Richard and Chantemesse, are important. According to the latter observers 4 parts of slaked lime (milk of lime) in a 1000 of water destroys the bacilli in typhoid stools in less than half an hour; the same result could not be obtained with chloride of lime (1 to 1000) or corrosive sublimate (1 in 50,000).

In the *sunlight* they are killed more rapidly. Cultures in a dish exposed to sunlight were killed in one to seven days; in sterilised water exposed to sunlight they were killed in an hour. It has been shown that this action is due principally to the chemical rays: all the rays have this bactericidal action, but the rays having the smaller wave lengths have the greater effect. In sterilised distilled water few have been found alive in twenty days after their immersion.

In sterilised *river water* they disappear in forty-three to eighty-one days. *In ordinary well water* or *river water* they rapidly diminish in numbers, whilst the water bacteria at first increase and then diminish. Few typhoid bacilli were seen in one case on the thirtieth day; in another none were seen on the fourteenth day. In some cases it was found that whilst living typhoid bacilli had disappeared from the liquid they were still to be found in the sediment at the bottom of the vessel. In *distilled sterilised water* the bacilli show signs of degenerative changes, the protoplasm gradually losing susceptibility to stains, and the organism becoming thicker and plumper, more oval in shape (Curt Braem.). They have been found alive after 196 days. The typhoid bacilli can also grow in *milk*, and live on various food stuffs, as in *butter*, where they have been found alive a week after the date of inoculation.

Poison.—In old peptone cultures Brieger by his method found that a poison is present which produces in guinea-pigs quickening of the respirations and increased glandular secretions; the limbs are weakened and the animal lies down, the pupils become dilated, the respiration becomes feebler, diarrhœa comes on, and death occurs in twenty-four hours from the beginning. The poison causing these symptoms is a diamine, having a provisional formula $C_7H_{17}NO_2$. It is not always found in the cultivation of the typhoid bacillus. To compare with this Luff isolated from the urine of typhoid patients a ptomaine, the reactions of which are given in a tabular form alongside those of the ptomaine isolated from the cultures of the bacilli (*9a*).

	Ptomaine from Typhoid Urine (Luff) (61).	Ptomaine from Cultures, on Meat Peptone, of Eberth's Bacilli.
	Solutions gave	
With phospho-molybdic acid	A white precipitate	A white precipitate
Phospho-tungstic acid	*Nil*	*Nil*
Iodine solution	Brown precipitate	Deep brown precipitate
Tannic acid solution	Yellowish brown precipitate	Deep yellow precipitate
Chloride of gold	Dense yellow precipitate	Gold salt soluble
Picric acid	Dense yellow precipitate	Not stated (in the reference)
Chloride of gold and picric acid	...	Yellow precipitate
Platinum chloride	*Nil*	...

From the liver, kidneys, and spleen of a fatal case of typhoid Brieger and Wassermann (*9b*) obtained a glycerine extract which, after filtration through a Berkfeld's filter, gave a precipitate with alcohol. This, being further purified by reprecipitation and dried, yielded a grayish white powder soluble in water, giving a yellow solution which frothed on being shaken up and presented the chemical reaction of albumin. One decigramme of this powder, dissolved in 1 c.c. of water, when injected into the peritoneal cavity of a guinea-pig, caused paralysis of the hind limbs, feebleness, lowered temperature, and death. On examination the animal was found to be emaciated, the liver fatty, and the peritoneum reddened, its cavity containing a little fluid. The same results were produced by the injection of 5 c.c. of the blood serum obtained after death from a fatal case of typhoid.

Diagnosis of Typhoid Bacillus from Bacterium Coli Commune.—In 1885 Escherich pointed out that in the normal stools of infants at the breast, a straight bacillus, of length varying from 1 μ to 5 μ and of a breadth of 0·3–0·4 μ was constantly found. The bacilli stained well with ordinary dyes, but not with Gram's method. In peptone sugar culture the bacilli were easily obtained, and fermentation took place. These bacilli when grown on gelatine do not liquify it. The deep colonies on plates have the appearance of very small yellow granular discs; the superficial

colonies form whitish lateral expansions of a uniformly granular aspect, sometimes iridescent; the outline is sometimes circular, but generally irregularly notched and wrinkled.

In drop cultivations the bacilli have a slight motility. On potato they form a juicy layer varying in colour from a greenish yellow to a maize-yellow. Milk is coagulated by these bacilli. Cultures of them are pathogenetic in guinea-pigs and rabbits; when injected into the jugular vein they produce diarrhœa, lowering of the temperature, and death in three days. On post-mortem examination the small intestine is in its upper part hyperæmic; the cæcum normal. The contents of the small intestine consist of a serous alkaline fluid, and the mucous membrane of the injected part is hyperæmic, soft and swollen; the Peyer's patches are swollen as in typhoid fever.

This bacillus being constantly found in the stools of persons in health was termed the bacterium coli commune. On account of its great similarity in size, shape, mode of staining, and growth on gelatine, to the bacillus described by Eberth (typhoid bacillus), other differential tests were sought for than those given by Escherich as distinctive of his bacillus (46).

Typhoid Bacillus (Eberth, Gaffky).	*Bacterium coli commune (Escherich).*
1. *Size*, length 2–3 μ, breadth 0·7–0·8 μ (Gaffky).	1. *Size*, 1–5 μ length, 0·3–0·4 μ breadth.
2. Has active movements.	2. Movements more sluggish.
3. Has 10–12 flagella (Nicolle and Morax), 18–24 (Rémy and Sugg).	3. Has 8–10 flagella more fragile than those of typhoid (Nicolle and Morax). 1–3 (Luksch). 4–6 (Rémy and Sugg). *Note to* 3.—Some of my specimens of bacteria coli commune have six flagella, most have only two or three. They appear to be very easily broken off. The bacilli adhere very tenaciously together in agar cultures. In drop cultivations a better result is obtained, but even then the number of flagella varies much more than in the specimen of typhoid. The bacillus was from a diarrhœal stool. The diagnosis by flagella may be made from my specimen.—J. R.
4. Produces no indol in peptone water inoculated with it when kept at 35° for forty-eight hours. (To 10 c.c. of the culture 1 c.c. of a 0·02 per cent solution of potassium nitrite is added, and one or two drops of pure sulphuric acid; *in the presence of indol*, a violet-pink colour is produced (Kitasato)).	4. Indol produced in forty-eight hours at 37° in peptone water.
5. Causes no formation of gas in media containing sugar, for example, 2 per cent sugar bouillon, 2 per cent sugar agar, etc. (Smith).	5. Causes abundant evolution of gas in media containing sugar.
6. No evolution of gas in gelatine "shake cultures" (Klein).	6. Bubbles surrounding the colonies in gelatine "shake cultures."

7. Does not curdle sterilised milk (Chantemesse and Vidal).	7. Curdles sterilised milk.
8. In cultivations in neutral whey an acidity equal to 2–3 per cent in volume of $\frac{1}{10}$th normal sodium hydrate solution is produced (Petruschky).	8. In similar cultivations an acidity equal to 7–8 per cent of alkali is produced.
9. Growth typical on potato acidified with 0·3–1 per cent solution of tartaric acid or monosodium phosphate (Ferrati).	9. Growth on potato thus acidified — *a thick yellow layer* (Ferrati).
10. Grows more slowly on gelatine.	10. Grows more quickly on gelatine.
11. Does not split up amygdaline in bouillon (Péré).	11. In bouillon cultures amygdaline is split up into glucose and hydrocyanic acid (Péré).
12. In fresh bouillon an acid reaction remains for some days (Péré).	12. In fresh bouillon the reaction, at first acid, becomes alkaline in five days (Péré).
13. Does not grow in bouillon containing $\frac{1}{7000}$th part of formalin (by volume) (Schild).	13. Grows in bouillon containing $\frac{1}{7000}$th part (by volume) of formalin (Schild).
14. The surface of gelatine upon which typhoid bacilli have already grown no longer grows them when again inoculated (Wurtz).	14. Will grow on a stratum of gelatine on which typhoid bacilli have previously grown (Wurtz).

Klein says the colonies of typhoid bacilli are iridescent, those of bacillus coli communis are not, and that the latter bacillus is much smaller than the former.

For practical purposes the distinction of the two bacilli must be made by means of the tests 4, 5, 6, 7, 9, and 13. By these tests we can ensure the similarity of the conditions of growth; and, if a micro-organism similar to that of Eberth in its morphology and gelatine plate cultures gives also these reactions of Eberth's bacillus, it is extremely probable that the bacillus in question is identical with that of Eberth.[1]

Examination of Stools. — Three volumes of the stool are mixed with one volume of 1 per cent solution of phenol in order to provide a mixture

[1] Since the above paragraph went to press a method has recently been published by Elsner (*Zeitsch. f. Hygiene und Infections Kr.* vol. xxi. 1895), which appears to fulfil the long-felt want of easily isolating the bacillus of enteric fever and to distinguish it from the bacterium coli. As the cultivating medium acid potato gelatine is used, after Holz (*Zeitsch. f. Bacteriologie*, vol. xiii.), to which 1 per cent of iodide of potassium is added. On this medium very few microbes grow; among them are both the bacillus of enteric fever and the bacterium coli; they grow, however, in so different a manner, that in the course of forty-eight hours the two can be readily distinguished. The colonies of Eberth's bacillus appear as small shining masses like drops of water; those of bacterium coli appear as coarsely granular, brown coloured collections of larger size. When the colonies are very closely set it may happen that the colonies of bact. coli, being checked in their growth, resemble those of the Eberth's bacillus, but if so, further plate cultivation will show the difference at once. In fifteen out of seventeen cases of enteric fever the bacillus was easily isolated from the fæces in the various stages of the disease. The importance of this method for clinical purposes, as it enables an observer, without being an expert bacteriologist, to isolate the bacillus of enteric fever from the fæces within forty-eight hours after inoculation, is shown by the observations of Lazarus (*Berlner klinische Wochensch.* 1895, December 9th) and Brieger (*Deutsche med. Wochensch.* 1895, December 12th). The latter found numerous bacilli in the dejections of patients suffering from enteric fever at a time when the symptoms were still very obscure. During convalescence the bacilli rapidly diminished: in two cases they persisted after the fever had disappeared, and both cases were followed by a relapse.

containing a quarter per cent of phenol. This is left for three hours at a temperature of 21° C. Plate cultivations are now made in Petri's dishes (four plates of various dilutions) from this mixture, using a moderately large amount of the sample for the first inoculation. The gelatine used should contain 0·25 per cent of phenol.

The plates when set are kept for forty-eight hours in an incubator at 22°. At least ten of the colonies, which present a superficial irregularly bordered expansion somewhat like a fig-leaf, are chosen; and each is inoculated into a tube containing 2 per cent of sugar as a stab culture (or made into shake cultures with gelatine); the former are kept at 37° C. for twenty-four hours, and no bubbles should be produced if typhoid bacilli are present; the latter are kept at 21° C. for two or more days. The growth of the typhoid bacillus takes place along the track as well as on the surface. If the growth takes place only superficially, or is very slow, or if bubbles are produced, the typhoid bacillus is excluded.

The tubes which may contain the typhoid bacilli are next inoculated (*a*) in peptone solution (2 per cent peptone, 0·5 per cent sodium chloride), kept at 37° C. for forty-eight hours. To each is then added twenty drops of 0·02 per cent solution of potassium nitrite, and one or two drops of pure sulphuric acid when *no* violet-pink colour should be produced. (*b*) In sterilised fresh milk; this should not be coagulated after some days' stay in a temperature of 35°. (*c*) On a half of a potato, the other half of which is inoculated with an authentic typhoid bacillus. These should show no difference after incubation. By using this method Mr. Richmond did not succeed in finding typhoid bacilli in the stools of convalescence from typhoid fever in seven cases at periods of 5, 7, 8, 10, 15, 16, 23, 24, and 30 days after a normal temperature had been reached. In the course of the investigation it was noticed that some apparently typical colonies produced gas formation in saccharine media, others did not; of those which produced no gas some gave the indol reaction, but three did not. These three coagulated milk so that the typhoid bacillus was excluded. Thus either organisms must have been present in the stools very like Eberth's bacillus in all their reactions except that of coagulation of milk, or Eberth's bacillus may under certain circumstances acquire the property of coagulating milk, a property possessed indeed by some of the recent cholera vibrios, but not possessed by the young cultivations of the older specimens and some of the recent specimens.

Phenol kills those organisms which, by producing liquefaction of the gelatine, would interfere with the plate cultures, but does not hinder the growth of typhoid and some other bacteria.

The results of the examination of stools based upon the diagnosis of the typhoid bacillus before the introduction of the indol and fermentation tests are, therefore, not so valuable as those made afterwards.

Pathogenetic Nature of the Bacilli. — The typhoid bacilli fulfil the necessary conditions as the veritable cause of enteric fever, namely — they are found in living organisms, and in the organs of persons who have died of enteric fever, and in no other disease; they can be cultivated

outside the body; when inoculated into animals, lesions like those of typhoid fever are produced, and they are found in the organs of the animal so inoculated.

It now remains to give briefly the results of observations on these points.

1. *Typhoid Bacilli in the Living Patients.*

In the *stool* of the patient they are constantly found (Strpolansky and Stroganoff). Wratch found them in 90 out of 96 cases examined. It must be noted, however, that they are rarely found before the 9th day of the disease (Karlinski), they may disappear from the stools before the end of the fever and, according to the observation of Mr. J. Richmond (see above), they quickly disappear after convalescence has set in. Strpolansky and Stroganoff have in two cases observed them in the stool nine days and fifteen days after the temperature had become normal.

In the *blood*, taken from the finger tip or from a vein by inserting the nozzle of a small syringe, bacilli have very rarely been found, and cultivations have either given negative results, or have shown the presence of streptococci or staphylococci, indicating a mixed infection. In the blood taken from the *roseolar* eruption some observers (Neuhans in 9 out of 15 cases, Roux, Meisels) have found bacilli like those of Eberth.

The *blood* from the *spleen*, drawn off by means of a small syringe, has often given positive results (Meisels found them from the 9th to the 18th day of fever, Buschelt in 8 out of 15 cases; in 2 of these streptococci also were present).

In the *fœtus*, after abortion or premature labour in typhoid patients, the bacillus has repeatedly been found. They were present in various organs of the fœtus (Neuhans, Hildebrandt, and Ernst).

In the *urine* Eberth's bacillus has been found by Leitz in 2 cases out of 7 examined. Newman found them in some cases on the 10th, 16th, and 21st day of convalescence; they were present in 8 cases out of 48 cases examined. Bouchard found them in 21 out of 65 cases; the urine in these cases contained albumin, which on precipitation settled at the bottom of the test-tube (retractile albuminuria); 9 out of these 21 cases were fatal, and the bacilli were found in the kidney. As early as the 3rd day of fever they were found in the urine by Karlinski.

In the *sputum* of typhoid patients suffering from pneumonia they may occur (Chantemesse).

Lastly, in the *sequelæ of typhoid*. There are already a great many cases recorded where the pus of abscesses, chiefly in connection with periosteum or bone, which appeared long after the patient had recovered from the fever, contained living typhoid bacilli. In Sultan's case (86) they were cultivated from the pus of an abscess opened six years after recovery from typhoid, and in a case recorded by Buschke (11) twenty-seven years had elapsed. In many of the cases recorded other micro-organisms, chiefly streptococci and staphylococci, were found in addition to the typhoid bacilli.

2. *Typhoid Bacilli in the Organs after Death.*—They have been con-

stantly found in the Peyer's patches, mesenteric glands, spleen and liver; occasionally in the myocardium (Chantemesse), kidney and meninges, and very often in areas concerned in the various complications of typhoid fever: instances will be given under Symptomatology.

3. *Inoculation on Animals.* — As animals do not suffer from enteric fever (there is some doubt whether the well-known outbreak of enteric fever at Kloten in Switzerland was really due to meat derived from a calf suffering from enteric fever), it is not easy to produce a disease in its symptoms like enteric fever in animals by inoculation, as was found by Murchison and others who fed animals with matter containing dejections from typhoid fever. Now, however, we have abundant evidence that under certain conditions a disease not unlike enteric fever, with lesions resembling those seen in it and presenting typhoid bacilli in the various organs, can be produced by inoculating animals with pure cultures of typhoid bacilli. Positive results were first obtained by E. Fränkel and Simmonds by intra-peritoneal injections in mice, guinea-pigs and rabbits; and they found consequently enlargement of spleen, hypertrophy of mesenteric glands and of Peyer's patches, and typhoid bacilli in the spleen. Sirotinin and Beumer and Peiper, on repeating the experiments, came to the conclusion that the animals died, not from an infection, but from an intoxication by the soluble product of the bacillus, and that no growth or multiplication of the typhoid bacilli had taken place. Numerous experimenters (A. Fränkel, Fodor, Leitz, Chantemesse and Vidal, Sanarelli, Cygnoeus, Gilbert and Girode) have, however, since confirmed the observations of Fränkel and Simmonds. The experimental methods were varied, some (A. Fränkel) injected the bacilli directly into the stomach or duodenum after laparotomy, as done by Koch in cholera inoculations; others (Chantemesse and Vidal) used small doses of very virulent cultures, or diminished the resistance of the animal by injecting at the same time into the peritoneal cavity sterilised cultures of other micro-organisms — streptococci (Chantemesse), bact. coli commune (Sanarelli); but all obtained positive results: the bacilli were found in the various organs, and even in the fœtus after an abortion, thus showing conclusively that an infection, and not an intoxication only must have taken place.

Cygnoeus used a virulent culture which he injected into animals in various ways — intra-venous, intra-peritoneal — and into the duodenum or ileum after laparotomies; he also introduced the culture by the mouth and by inhalation. Many of the inoculated animals (mice, rabbits, dogs) died, and at the post-mortem the spleen and mesenteric glands were found swollen, and the Peyer's patches reddened. Bacilli were found in the spleen, the liver, the intestines, the kidney, and the medulla of bone. Positive results were also obtained with some of the mice which had inhaled cultures of bacilli.

The results of the experiments where other micro-organisms were introduced in order to weaken the resisting power of the organism receive a further confirmation by recent observations of Alessi, who found

that guinea-pigs made to breathe the effluvia from cesspools were killed by feeble cultures of typhoid bacilli which had no action upon animals of the same size kept under more favourable conditions.

Relation between B. Coli Com. and Typhoid Infection. — Pisenti and Biancho-Mariotti found — 1. On simultaneously injecting into animals cultures of typhoid bacillus and B. coli com. (which latter had been proved to be inactive), that B. coli com. increased in virulence, so as to act like very virulent B. typh. on animals.

2. That if sown in gelatine mixed up with filtered cultures of B. typh., B. coli also gains in virulence, which is due to typho-toxin acting on the B. coli.

3. That healthy intestinal epithelium hinders infection from the intestine; but that if Peyer's patches undergo changes this defence is in abeyance. Filtrates from typhoid cultures exert an influence on Peyer's patches, as proved by experiments (nature not stated), so that in typhoid fever the toxin in the blood alters the Peyer's patches, and thus B. coli are permitted to get into the body and add to the virulence of the typhoid infection.

4. That the virulence of B. coli is increased by simultaneous injections of streptococci pyo. aur. (explaining Vincent's observation that typhoid is more severe when streptococci are present in the blood).

5. That with very virulent cultivations of B. coli they could get similar results (such as thermometric curves, for instance) to those obtained by very virulent B. typhoides, and could immunise animals against B. typhoides; at the same time they guard against any expression of opinion as to the identity of the two.

Ways of Infection. — Having shown that the typhoid bacillus is the immediate cause of enteric fever, we may now consider by what channels it may be conveyed. The general conclusions as to the etiology of enteric fever arrived at by many years of experience and observation before the discovery of the typhoid bacillus were — that it occurs in sporadic cases or in epidemics; that the poison is contained in the alvine discharges of the typhoid patients, contact with which may communicate the disease to a healthy person; that an outbreak of enteric fever implies poisoning of air, soil, drinking water, milk, or other ingesta with the fever poison. In some cases the source of the poison cannot be traced, hence, as I have already said in the short historical sketch at the outset of this article, many have believed that typhoid fever may arise spontaneously.

In some instances it is no doubt very difficult, often even impossible, to trace the origin of a case of enteric fever, or to explain the source of an outbreak of the disease; but considering the long vitality of the typhoid bacillus under certain conditions, its probably wide distribution, its rapid multiplication, the great dilution to which it may be subjected without losing its potency — as shown in some epidemics, where the source of infection was undoubtedly proved, as in the outbreak at Lausen (12) — and the influence which the presence of other micro-

organisms and impurities of the air have either in favouring its development, or in diminishing the power of resistance of the individual, we can quite understand that it may often be difficult to trace the source of infection. Is there not the same difficulty in other infectious diseases, such as small-pox or scarlet fever; yet no one believes in the spontaneous origin of these affections?

The typhoid bacillus is contained in the dejections of the typhoid fever patient, and "typhoid fever" is chiefly propagated by these.

It is stated by most observers that fresh typhoid stools are not infectious (Murchison, Caley), and that they only become so after one or more days. If this be so, it could be explained readily by the observations of Hüppe, who found that the typhoid bacilli in recent stools being anaerobic when leaving the body, were more influenced by external agents than bacilli found in stools that have stood for some time and have thus become aerobic (41).

We have seen that the bacilli are occasionally contained in the sputum and in the urine; these secretions, therefore, cannot be neglected as sources of infection, and should be thoroughly destroyed.

The paths of conveyance are —

1. Direct contact with particles of dried fæces contained in the clothes of the patient, bed linen, etc.; many instances have been recorded where washerwomen, nurses, and others have been infected in this way.

It is also quite possible that insects, such as flies, may carry infectious particles from typhoid patients to fruit and vegetables. This mode of infection may explain the occurrence of some sporadic cases. We know that the bacillus grows well on many vegetables besides potatoes and other articles of food (39); and on the other hand, experimental observations by Hoffman and others have shown that both cholera bacilli and tubercle bacilli may be conveyed by flies; Burgess has recently given further proof how easily micro-organisms may be conveyed by flies. With other articles of food taken raw — such as milk, oysters, watercress — which are now known to be a source of infection, contamination is due to the water. Infection by oysters has been recently observed in London and elsewhere (10), and cases like those observed by Sir Wm. Broadbent seem to prove that oysters not infrequently act as carriers of the poison.

2. Water into which the excretions find their way. This may be drinking water, or water used for rinsing milk-cans, etc., which may thus give rise to epidemics, when the disease is propagated by milk; or, as in one or two outbreaks recently recorded, by ice cream: vegetables, again, may be washed in contaminated water; or oysters may contain it (see above).

3. Air. This is now known to be a very rare mode of infection. It is, however, not impossible that dried bacilli may be suspended in the air. Tryde and Salomonson found typhoid bacilli on the floor of a barrack where enteric fever was prevalent. (It is doubtful, however, whether these were proved to be typhoid bacilli.) Lassurie (54) passed a pulverising spray of water over a quantity of dried typhoid bacilli, and found

that the particles of spray carried the bacilli some distance. The part played by sewer air will be alluded to later.

4. Food from animals affected with the fever. Several such epidemics have been recorded, whether actually enteric fever or not. In the one at Kloten the affected person not only partook of the meat (supposed to have been derived from a calf suffering from typhoid), but also partook of wine and other drinks. It is very probable that the beverages consumed contained the active agent, the action of which would be assisted by the putrid condition of the veal. Enteric fever, moreover, has not been recognised in animals.

It would be beyond the scope of this article to go fully into the various outbreaks of enteric fever and their respective sources, which subject is fully treated in works on hygiene and in larger treatises on enteric fever, as in one just published (9*c*).

The facts ascertained with regard to the outbreaks of typhoid fever are, briefly, that in very few cases is there any evidence of direct contagion from the sick to the healthy; in a considerable number of cases, especially of isolated cases, no direct or indirect contagion can be proved; in a large number of cases, especially in large epidemics, the disease arises among persons who drink unfiltered and unboiled water or milk contaminated with typhoid stools.

Enteric fever due to *milk* contamination is chiefly confined to houses served by a particular dairy; the attacks are simultaneous, and confined at first to those members of the family who had partaken largely of unboiled milk, especially the younger. As a rule the cases have not a high mortality. In many of them it has been proved that enteric fever existed at the farms from which the milk was derived; that the water-supply of the farms was infected with the stools, and that the milk cans were washed with the infected water. As fresh warm milk is a favourable medium for the growth of the typhoid bacillus, a small amount of infected material would contaminate a large amount of milk.

In epidemics from the use of *contaminated water*, the cases arise to a much greater extent among those who use the suspected water than among those who have another water-supply (6), the percentage of attacks not being very high; or severe outbreaks arise in connection with the consumption of water from a particular well contaminated with typhoid stools, as in Budd's Cowbridge case, where of 140 persons who possibly might have drunk of water from a well polluted with typhoid stools forty or fifty had typhoid fever — some after a very short period of incubation. In the Tees valley outbreak a large body of water was contaminated: in the former one a small body was more intensely infected, and a very large percentage of consumers were attacked. In these cases bacteriological examination of the water may be carried out in the way recommended for the examination of stools; or the first step by which the liquefying organisms are got rid of may be attained by Parietti's method. In this method three, six, and nine drops of a solution of 5 per cent phenol and 4 per cent of hydrogen chloride in distilled water are

added to tubes, each of which contains 10 c.c. of neutral bouillon. These are capped and kept at 37° in the incubator for twenty-four hours. The tubes which have become turbid are now excluded. To each clear tube are then added one to ten drops of the suspected water, according to the amount of impurity. The tubes are capped, shaken, and incubated for twenty-four hours. Plate cultures are now made from the turbid tubes.

Other methods have also been formulated and described in bacteriological text-books: when the infecting material is largely diluted, or the examination is made some time after the fouling has occurred, the typhoid bacillus may not be detected, and bacterium coli only found. In these cases a much larger quantity of water must be examined; this can be effected by passing a large quantity of the water through a sterilised Chamberland's porcelain tube contained in a sterilised stoppered vessel, as suggested by Professor Delépine; the scum collected on the outside of the tube is afterwards to be examined bacteriologically. Typhoid bacilli have often been found in water which has been consumed by persons who have suffered from enteric fever: in some of these cases the water has been derived from wells into which cesspools containing such stools have drained; in others the water of rivers or brooks has been contaminated by sewage, by drainage from fields manured by privy refuse, or by drainage from laundries where clothes soiled by typhoid stools have been washed. In conducting bacteriological examination of water, it must be borne in mind that a number of bacilli may occur in water, which closely resemble the typhoid bacillus both in appearance, in the character of the colonies, and even in some of the reactions; so that it becomes necessary to use every one of the differential tests given above: indeed in the present state of our knowledge, even if the organism do present the various test reactions we can then only say that it is like the typhoid bacillus. For further references on the subject we refer to Lustig's treatise (63). In many of the cases in which enteric fever has been associated with the use of a particular water-supply, some of the persons exposed to the infection have escaped; in other cases persons living in particular districts have scarcely suffered, whilst in other districts having the same water-supply the fever has been very prevalent. Thus there is a local immunity as well as an individual immunity. Chantemesse points out that the 20th arrondissement had in the ten weeks beginning with the 20th February 1894 a mortality from enteric fever of 0·5 per 10,000; whilst in the 17th, 18th, and 19th arrondissements, inhabited by the same classes of people, and where the same water was drunk, the mortality was 0·88 per 10,000. The same arrondissement for the last thirty years has had a lower mortality from enteric than the mean mortality of the other arrondissements of Paris (50). The Tourelles barracks did not present a single case. The water-supply, examined on the 6th April, yielded bacilli coli commune — probably, but perhaps not necessarily, due to fæcal contamination — but no typhoid bacilli. The 20th arrondissement has a less crowded population and more open spaces than the others, except in Belleville which,

though thickly populated, is situated on a well-ventilated and elevated site. On this subject Mr. Hart's articles on Water-borne Typhoid in the *British Medical Journal* for 1895 may be consulted.

Fodor found that the mortality from typhoid fever in Buda-Pesth was greater in those houses which were supplied by well water than in those supplied by pipe water (filtered); and greater in those houses where the ground water was more impure, and where the ground was more polluted with organic matter which did not present evidence of active oxidation.

In Dublin, which has a pure water-supply, but where the soil is saturated with the filth from privies and ashpits formerly in use, those living on clay suffered much less from enteric fever than those living on the porous gravel; and Sir C. Cameron believes this difference to be due to emanations from the filthy soil. At Stockport the grouping of cases of enteric was noticed in three particular areas, the three highest points in the town at which the sewers were ventilated. This association has been noted elsewhere. In many cases insanitary conditions allowing sewer gas to pass into houses are found where this fever occurs. Instances might be infinitely multiplied. Thus impurity of the soil and the breathing of sewer air are often found in connection with enteric fever, but there is no exact evidence that these act otherwise than as accessory agents. There is no evidence that sewer air contains typhoid bacilli; it is found that in well-ventilated, well-constructed sewers the air contains fewer bacteria than the outside air; but where the sewage is stagnant it is possible that gas abundantly produced by the formation and the bursting of bubbles may disseminate solid particles in the air, and some of these may be wafted up into those houses where the soil-pipes act as sewer ventilators, or into the air about the ventilating grids. In some of these ways it is possible to explain the origin of cases which appear obscure without invoking the action of any miasma, except as an adjuvant cause as in Alessi's experiments.

This brings us to the consideration of *remoter causes* which favour the occurrence of the disease. Of these may be mentioned —

1. *Age.* — Enteric fever occurs much more frequently amongst the young, and adult persons under 35. It is not uncommon in children, but very rare in infants. This will be evident from some of the tables which accompany this article.

2. *Sex.* — The male sex appears, from the number of cases admitted into hospitals, somewhat more disposed to the disease than females. Thus there were admitted into Metropolitan Asylum Board's Hospitals in the years 1871–1892, 3293 males and 3030 females between the ages of 10 and 35 years. But probably more males are admitted into hospital than females, so that the liability to enteric fever may be the same in the two sexes.

3. *Season.* — Though enteric fever occurs at all seasons, it is much more prevalent in autumn and beginning of winter, especially after a dry and hot summer. In London the maximum mortality is in November;

in England the maximum prevalent in October. This seasonal prevalence must be due to some meteorological influence; but the favouring conditions of temperature, atmospheric pressure, and rainfall are not definitely known.

Pettenkofer and Buhl pointed out that in Munich the maximum prevalence of enteric coincided with the lowest recession of the ground water from the surface of the soil, and was especially marked when the ground water was previously high. These are just the circumstances favourable for the pollution of wells by filthy soil, as Buchanan has pointed out. Fodor showed that at Buda-Pesth the maximum of the prevalence of the fever coincided with the maximum height of the ground water, that is with the highest level of the Danube. The same observation was made by Thorne Thorne in an outbreak of the disease in Jerling, Essex.

In many places Pettenkofer's observations have been confirmed, in many they have not; moreover, as Flügge (27) points out, the number of cases in the quarter of the year in which the ground water is at the lowest level, compared with the average number of cases in the other quarters, shows only a difference amounting to 10–20 per cent of the total number of cases (17 per cent in Berlin); so that the sinking of the ground water only increases the number of cases by a small fraction of the whole, the rest occurring during the rising and the high level of the ground water.

English observations have led to the conclusion that a permanent low level of the ground water (at depth of 15–20 feet) is the best for health.

4. Defective drainage and sewerage, accumulation of filth, overcrowding and disregard of ventilation, in fact, all shortcomings in sanitation of the individual and of the community are most important agents in favouring the power of the typhoid bacillus, and in lessening the resistance of the individual. The improved sanitary condition of most of the English towns as regards water-supply, sewerage, open air spaces, etc., is the chief cause of the diminished mortality. This diminution amounted to 45·4 per cent in twenty-one out of twenty-four English towns; in three towns where the typhoid mortality was increased, the sewerage arrangements were manifestly faulty. (See accompanying table giving the annual mortality from typhus and typhoid per million persons living, in England, Table I., Appendix.)

5. Other less potent causes are peculiarities of constitution (see under Prognosis), and recent residence in an infected district. Occupation and station of life have no influence.

Immunity. — We will confine ourselves entirely to a few facts in relation to this subject, the general consideration of which is dealt with elsewhere.

Some persons show a natural immunity from enteric fever; acquired immunity is a well-established fact in this as in some other infectious fevers. Of over 2000 cases of enteric fever which came under observation at the Hamburg General Hospital, only fourteen persons were affected twice, and only one person three times by enteric fever. Of the

experimental investigations we may briefly allude to the observations of Widal and Chantemesse, Brieger, Kitasato, Wassermann, and Stern.

In the course of these investigations it was found that when cultures of typhoid bacilli which were virulent, or which had been sterilised by heat, were used to infect animals, and the animals survived the action of the virus, that these animals were more or less immune to the action of a stronger virus. By regulated doses of the weakened virus injected subcutaneously (or in some cases into the veins) guinea-pigs were rendered immune from the action of a stronger virus. The blood serum of these guinea-pigs was then found to confer immunity upon other animals when used in the same way, and to retard the disease in animals already affected. According to R. Pfeiffer, if the serum of a highly immunised guinea-pig be injected with a small dose of typhoid bacilli into the peritoneal cavity of a normal guinea-pig, and drops of the peritoneal exudation then removed for examination, the bacilli are seen rapidly to undergo degenerative changes, and finally to disappear. Other bacteria when subjected to the same process remain unaffected. Hence this "specific immunising power" of the serum in question may be used as a diagnostic test for the typhoid bacilli (68*a*). Dunbar confirms Pfeiffer's results (21*b*). It is obvious, however, that if moderate doses of the bacilli to be tested will not grow in the peritoneal sac of a normal guinea-pig the reaction will not be available. The blood serum of men who have enteric fever, and of some who have not had it, has the same property (Stern). The serum of protected guinea-pigs injected subcutaneously in the enteric fever patients gave no important results (Chantemesse).

Fränkel and Simmond's observations with sterilised cultures of typhoid bacilli will be referred to under Treatment.

Portals of Entrance into the Human Body of the Typhoid Bacilli. — The digestive tract forms the principal channel along which the typhoid bacilli find their way into the body. This is evident from the well-established fact that from the post-mortem appearance most outbreaks can be traced to contaminated water or milk. Chantemesse quotes a case of Klebs, where a man died on the second day of the disease, and in the mucous, submucous, and muscular coat of the intestines masses of typhoid bacilli were found. From what has been stated before, it is evident that typhoid bacilli may find their way into the air, and may thus enter by the respiratory tract. Yet it is quite possible that they may be arrested in the pharynx, and thence find their way into the digestive tract. Wyssokowitch was not able to find typhoid bacilli in animals which had inhaled dried culture of typhoid bacilli, or in which he had injected typhoid bacilli into the trachea. The occurrence of pneumonia at the very onset of entric fever, and the presence of typhoid bacilli in the lungs in these cases, make it not improbable that occasionally, though no doubt very rarely, the bacilli may enter the system through the respiratory tract.

Recently Anderson described two cases of enteric where the fever

was contracted in the hospital, and where there was presumptive evidence that the infection was conveyed by an enema syringe; the entrance in this case would be per rectum.

Symptomatology. — The symptoms of enteric fever vary considerably in individual cases both as regards character and intensity; this is due partly to the intensity and localisation of the poison, and partly to a mixed infection by septic organisms. It will be well to describe at first an ordinary case, then to give an analysis of the symptoms and of the complications, and the sequelæ. In each case of enteric fever we may take certain periods to represent the several stages of the affection. The following stages are recognised by most clinicians: incubation, onset or invasion; the fever period itself, which is divided into the first, second, and third week of the fever — or, according to Murchison, into the stage of glandular enlargements extending to the 12th or 14th day, the stage of ulceration or sloughing of the intestinal glands extending to the end of third week — lysis, or gradual diminution of the fever, and convalescence.

The *incubation period* varies considerably; it seems in most cases to be about fourteen days; in some cases, however, it has been ascertained to be as short as four or five days, or even shorter; in others it may extend over three or four weeks. During the period the patient may either experience no symptoms whatever, or, as is most commonly the case, towards the end of this period, he may complain of headache, loss of appetite, sleeplessness, and a sense of fatigue; this stage may gradually pass into the next stage.

The Onset. — In many ordinary cases the onset is insidious. The patient complains of pain in the limbs, of excessive fatigue, of cold and chilly sensations, of headache often very severe, of loss of appetite, and of sleeplessness: epistaxis is a very common symptom, and generally occurs about the second or third day of the disease. These symptoms become more severe, the patient has to take to his bed, and from this day we generally reckon the duration of the fever. In many cases, however, as shown by the changes after death, the beginning of the morbid process must be dated from the very first symptom. The tongue becomes furred, and is at first moist; there is a steady rise of temperature, the evening temperature being generally one and a half degree (F.) higher than the morning temperature, so that about the fourth day the temperature reaches 103° F. or 104° F.; the pulse rises to 90 or 100, rarely higher except in very severe cases, or in very young or debilitated subjects, is dicrotic and indicative of low blood pressure; there is increased thirst; the abdomen is slightly distended and tender on pressure; diarrhœa may as yet be absent, and there may be constipation, or there may be two or three fluid stools from the first. Beyond the headache, which persists for a few days, and sleeplessness, there are as yet no other symptoms; the skin is dry, but there are paroxysms of profuse perspiration. The spleen is as yet but little enlarged, and there are as yet no roseolar spots, though when perspiration is profuse sudamina are noticed; the urine has

febrile characters and as yet does not show the diazo reaction. This stage lasts about seven days, and constitutes the first week of enteric fever.

During *the second week* more characteristic symptoms appear. The fever remains high and steady, the morning remissions being less; the pulse is quicker; the skin remains moist; the tongue becomes dry and brown, and the lips likewise; the roseolar rash appears, between the seventh and twelfth day, in the form of isolated, circular, rose coloured spots, slightly elevated, and about the size of lentils, from two to four millimetres in diameter, disappearing on pressure, and reappearing with the removal of the pressure; they appear chiefly on the abdomen and back, occasionally on the arms and thighs; they may be very few in number, or at times very numerous, and they appear in successive fresh crops, while the old ones gradually fade: the appearance of the spots continues up to the end of the second week, and often to the middle or end of the third week, or even during convalescence. In some cases a minute vesicle may be seen at the apex of the roseolar spot. During this stage the abdomen becomes more distended, gurgling in the right iliac fossa is noticed, and the abdomen may be painful on pressure. The diarrhœa is now more profuse, and the motions have the characteristic pale yellow ("pea-soup") colour, and, especially in children, are highly offensive. The spleen is now considerably enlarged, is often to be felt below the costal margin, and is occasionally painful on pressure. The respiration is quickened, but not as quick as in pneumonia; still there may be some bronchial affection with mucous expectoration. The temperature during the first few days of the second week continues high, with marked evening exacerbations. About the middle of the second week, in moderately severe cases, the morning temperature is lower than it was before; in others the morning remission is but slight, and the fever has a less remittent character; in very mild cases the fever may disappear about the end of the second week. The urine is scanty, high coloured, and of high specific gravity; occasionally it contains albumin, and in most cases gives the "diazo reaction." The headache usually disappears during the second week if not before; there is often marked and increasing deafness. The patient in the second week, except in very slight cases, assumes a somewhat characteristic appearance. He is dull, apathetic, and has a heavy look; the face is pale, the cheeks occasionally flush, the pupils dilate, and the lips are dry. In severer cases there is delirium, especially at night, and in still more severe cases other nervous symptoms (constant delirium, somnolence, subsultus tendinum) may supervene, and death may take place during the second week. Hæmorrhage from the bowel occasionally occurs towards the end of the second week.

During *the third week*, in mild cases, the symptoms gradually subside. In moderately severe cases most symptoms remain the same as during the second week; but the temperature shows marked morning remissions, and the fever gradually declines, and may show for a few days an intermittent fever type, — the morning temperature being normal, the evening temperature still reaching 100° F. or 101° F.; in more severe cases the

temperature may remain high and even increase, the pulse becomes smaller and quicker, the tongue quite dry and brown and often fissured, the lips covered with sordes, the diarrhœa persistent, and the perspiration profuse: the delirium is now constant, and often of a low, muttering, or sometimes of a violent maniacal character; the loss of flesh becomes particularly apparent during this week, and bed-sores may appear if the nursing be inefficient. Hæmorrhage from and perforation of the intestines are apt to occur during the week. Pulmonary complications and failure of the heart's action are to be feared, and would show themselves by quick and small pulse, cyanosis of the face, clammy perspiration, and the like; other unfavourable symptoms relating to the nervous system may also occur towards the end of the third week, such as retention of urine, or involuntary discharge of urine and fæces.

With the *fourth week* convalescence commences in ordinary cases, in very severe cases later. The evening temperature now falls gradually to the normal, or nearly so; save a few exceptions (Fagge, Morris), there is no crisis, but a gradual defervescence; the alvine evacuations become formed, the pulse improves, and the tongue begins to clean, while the appetite returns and becomes almost ravenous; the pulse becomes slower and firmer; there is often polyuria, the urine having a low specific gravity; the nervous symptoms quickly disappear; the sleep becomes more natural, and though the patient feels excessively weak, often complains of vertigo and palpitation, and is pale and anæmic, the strength gradually returns and is maintained; unless the convalescence be interrupted by *relapses*, or some of the sequelæ to be mentioned below ensue. In very severe cases the fourth week often brings not only no relief, but even an aggravation of the symptoms of the third: the pulse may reach 140 or more, the respirations become laboured, the face is dusky and covered by clammy perspiration, urine and fæces pass involuntarily, and coma gradually sets in, soon followed by death: some few patients, however, in spite of the severity of the symptoms, take a favourable turn, and eventually recover. Convalescence begins in the majority of cases with the fourth week: in not a few cases, however, the fever does not subside till the end of the fourth week; whilst in some protracted cases it may continue during the fifth or even the sixth week.

The above is a brief description of the symptoms in ordinary cases of enteric fever. Certain variations both in the onset and course of the disease are, however, sometimes noticed.

As regards the onset, it is well to know that occasionally this may be sudden, in one of the following ways—(*a*) Symptoms resembling an ordinary febrile cold: repeated shivers, with headache and rise of temperature; but a single rigor, so characteristic of pneumonia, is very rarely seen in enteric fever. (*b*) Symptoms resembling acute gastritis: such as frequent vomiting, which may persist for a few days, and be soon followed by diarrhœa; the gradual increase of the temperature, which on the fourth day may reach 103° or more, assists us in diagnosing such a case from gastro-intestinal catarrh. (*c*) In other cases the patient at

first complains of sore throat, and the tonsils may be so swollen as to interfere with breathing and swallowing; the accompanying headache, epistaxis and pyrexia here assist us to make an early diagnosis. (*d*) The first symptoms may be those of pneumonia, and only after some days the typhoid symptoms (diarrhœa, enlargement of spleen, roseola) present themselves. These cases are known as pneumo-typhoid, and, as in some of them the typhoid bacillus has been found in the pneumonic lung, we have probably here to do, in some cases at least, with enteric fever in which the typhoid bacillus established itself first in the lungs; in other cases we probably have to do with two coincident affections — pneumonia and enteric fever (Chantemesse). (*e*) The fever may set in with severe headache and vomiting, soon followed by delirium, retraction of the head, and photophobia, — indeed with all the symptoms of meningitis; and it is only after five to six days that the true nature of the case reveals itself: this onset is not rare in children. (*f*) Symptoms of acute nephritis (nephro-typhoid) (see below). (*g*) In very rare cases laryngeal symptoms (laryngo-typhoid).

During the stage of glandular enlargement the temperature may not show the characteristic curve; it may be normal, or but little above normal, throughout the whole course (apyrexial type), or slightly febrile (in mild cases), or it may show great variations; again diarrhœa may be absent throughout the whole course, or there may even be obstinate constipation. Grave nervous symptoms may persist throughout the whole period, as in the form of constant delirium or drowsiness; the presence of the other symptoms characteristic of the disease helps us in the recognition of these aberrancies. As the symptoms vary considerably in some cases, I will now give a brief analysis of the symptoms relating to the various organs.

Temperature in Typhoid. — For the majority of cases the observations of Wunderlich on the temperature curve in enteric fever still hold good. With the onset the temperature rises gradually during the first four days, an evening exacerbation of about 1·5° to 2° F., being followed by a remission next morning of about 1° F., so that there is a gradual mean rise with a daily zig-zag, the summit of which reaches about 103·5° to 104°, on the fourth day. This is followed by the fastigium, lasting for about seven days, during which time the temperature is more uniform and of continuous type, the morning temperature being 102° to 103°, evening temperature 103° to 104° F. In many cases there is on the seventh day a distinct but only temporary fall of a few degrees. From this point to the end the temperature varies with the severity of the case (excluding such accidents as hæmorrhage); in ordinary moderately severe cases the temperature, after the eleventh or twelfth day, has for three to four days a remittent character, the morning temperature now falling, and more rapidly than the evening temperature; during the remaining days (from about the sixteenth to the twenty-first) it assumes an intermittent character, the morning temperature being about normal, the evening temperature reaching 101·5° to 101°, and coming somewhat

rapidly down to the normal on the twenty-first day: in mild cases the temperature may fall more rapidly at the end of the second week, and may reach the normal soon after; in severe cases the morning temperature remains high after the second week, between 103° and 104°, and the evening temperature reaches 105°; or we have irregular temperatures for several days after the twelfth day (the "amphibolic stage" of Wunderlich, the "stage of changing fortunes" of Murchison). Defervescence thus takes place more or less gradually; but sometimes the fever may terminate by sudden crisis on or before the end of the third week. For the majority of cases, then, Wunderlich's observations on the temperature hold good, and from a diagnostic point of view it is well to remember his general rule: — Any fever which on the second day reaches to 104° F. is not enteric fever, nor is it enteric if the fever does not approach 104° F. on the evening of the fourth day; on the other hand, enteric fever may be diagnosed, if in a middle-aged person suffering from an acute febrile attack the evening temperature on the fifth day, or within the first week, is between 103° and 105°, and alternates with morning temperatures, which are 1·4° to 1·7° lower, unless some other disorder can be discovered to explain the height of the fever. It is well to state that by morning temperature we mean the temperature about 9 A.M., by evening temperature that about 6 P.M. If the temperature be taken every two hours greater differences are sometimes noticed during the twenty-four hours.

There are, however, many variations of the temperature curve. Thus, sometimes, especially if pneumonia intervene, or even in simple cases there may be a very high temperature on the second day; again, we occasionally meet with hyperpyrexia, which may reach 109°, and even 110°. Such temperatures generally occur during the third week, and are quickly fatal; but temperatures between 105° F. and 106° F. may be met with even towards the end of the second week in cases which recover, especially in young subjects. Again the temperature may undergo sudden alterations from incidents which arise during the fever; thus an attack of pneumonia, occurring, as it often does, towards the end of the fever, causes a sudden rise of temperature; various septic affections, which so often complicate enteric fever, considerably disturb the fever curve;[1] hæmorrhage from the ulcers causes a sudden fall of the temperature; perforation of the bowel often has a similar effect; and even nervous symptoms, or failure of the heart, may be ushered in by a fall. Again

[1] It is stated by many observers that in persons who have had malaria the temperature in typhoid shows a distinctly intermittent type, accompanied by rigors and sweating, and the typho-malarial fever of the tropics has been looked upon by some as enteric fever. Osler and others have described cases where malarial fever came on during an attack of typhoid without the temperature becoming intermittent; and other observers (Purjez, Weil) (96) describe a true intermittent temperature in enteric fever without any malaria, which may persist throughout the whole course. (*Vide* art. "Fevers in India.")

In a few cases oscillation between high and very low temperatures has been recorded; thus in a child suffering from enteric fever the temperature fell from 101° F. to 91° F., and then gradually rose to normal. With the rapid fall of temperature signs of pneumonia appeared (71*a*).

the fever, instead of terminating at the end of the third or fourth week, may run on for weeks, protracted by a variety of causes, such as continued ulcerations, septic complications, etc.

Some cases of enteric fever may run their whole course without any rise of temperature, or with a temperature but slightly above normal, or even with a subnormal temperature. Such cases have been described by Gerhardt (34, 97) and myself (21). Even epidemics of such cases have been described (30). In two of the cases observed by me, not only were all the prominent symptoms of enteric fever present, with the exception of pyrexia, but there was also a distinct relapse, lasting in one case exactly three weeks, during which there was marked hæmorrhage from the intestines. The prognosis of these cases, in spite of their apyrexial nature, is as grave as that of ordinary enteric fever; one of my patients died from perforation, and the two cases described by Wendland terminated fatally.

Post-Typhoid Pyrexia. — Apart from the cases which are mentioned above, in which the temperature, on account of some complication or continued ulcerations, does not come to the normal for many weeks, we may note a rise of temperature lasting a short time; this occasionally happens during convalescence, and is sometimes referred to errors in diet, or too nitrogenous a diet, or to constipation (in one case the temperature ran to 105° after having been normal for three days, and quickly subsided again after an enema). Slight elevations of temperature during convalescence are often noticed in very anæmic persons or in those of highly nervous temperament (Osler).

From these post-typhoid temperatures must be distinguished the fever of the relapse, which will be described hereafter.

Symptoms on the Surface of the Body. — The roseolar eruption has already been described. It is present in about 77 per cent of the cases; it is more often wanting in children, but may be even copious in them. Of other eruptions which are met with we have to notice: —

(*a*) Maculæ cæruleæ, tâches bleuâtres, peliomata, blue tinted spots of indefinite size, situated chiefly over the abdomen; these appear to be caused by the irritation of pediculi, and occur in other febrile affections.

(*b*) Petechiæ or Purpura Spots. — In rare cases the typical typhoid rash may be accompanied by petechiæ; at other times, in badly nourished and debilitated persons, or when septic complications occur, petechiæ may appear at the height of the disease.

(*c*) Miliaria and sudamina are not unfrequently met with; they appear sometimes early, but generally in the second and third week of the disease; they are very numerous, and principally situated on the front and back of the chest and on the abdomen; the sudamina are small vesicles, filled with clear fluid, and are not likely to be mistaken for any other affection. This eruption, of course, occurs in many other diseases.

(*d*) Erythema. — A rash of vivid red colour, not unlike the scarlet fever rash, sometimes appears during the first week, chiefly on the chest and abdomen. I have twice noticed a similar rash occurring

during the third week, and chiefly affecting the arms. This rash may in some cases be due to the administration of drugs — quinine, salicylate of sodium, antipyrin, etc. It has been observed, however, quite independently of such drugs (65, 100), and is probably of septic origin.

(*e*) Morbilliform rash, resembling measles (58, 66), in larger or smaller patches, with a dark hæmorrhagic centre and a lighter coloured periphery, affects the neck and trunk, spreads rapidly, but does not extend to the mucous membrane, and appears not materially to affect the course of the fever. Neumann found the streptococcus pyogenes on the arms of a patient during the existence of this rash.

(*f*) Urticaria is occasionally observed, but is probably in most cases a drug eruption.

(*g*) Herpes, so common in pneumonia, is very rare in enteric fever; it has been observed sometimes, however, during the first week. In two cases in which I noticed it the enteric fever was complicated by pneumonia.

(*h*) Desquamation in fine branny scales is often observed towards the end of the fever or during convalescence.

Œdema of the skin is noticed sometimes towards the end of the febrile period (from thrombosis of a vein), or during convalescence (from anæmia and nephritis).

Erysipelas. — This is occasionally noticed as a complication. I have seen it twice in children; it occurred when the fever symptoms were subsiding. It commenced in the usual way — the face, forehead, and ears being chiefly affected, and it ran a favourable course. Silvestrini (81), in a case of erysipelas complicating enteric fever, found the typhoid bacillus in the erysipelatous eruption.

Bed-Sores. — The marked improvement which has taken place in the nursing and management of fever patients has almost abolished bed-sores; yet in a few very protracted cases in very debilitated persons, whatever the precautionary measures, they may perhaps be unavoidable; and several factors, besides mechanical pressure — such as the condition of the blood, and trophic changes due to central nervous causes — help in their production. They are noticed over the sacrum, or over the trochanters, knees, elbows, ankles, shoulder, head, etc. At first the skin reddens, then small superficial erosions or fissures appear, and these deepen, giving rise to gangrenous patches, which may slough off, leaving the subjacent parts bare; occasionally the destruction of tissue extends, and may be accompanied by suppuration and the appearance of septic symptoms. We may thus have extensive destruction of bone, which, when it affects the sacrum, may lead to septic meningitis, or when the bed-sore is situated over a joint may lead to opening of the joint cavity, and further changes.

During convalescence one notices occasionally *loss of hair*, which, however, in most cases grows again. As in other fevers and severe diseases, a transverse *ridge of the nails*, from interference with nutrition, is noticed after recovery from enteric fever. There is an opaque white

line, followed usually at some little distance by a depression; starting close to the bed of the nail, gradually with the growth of the nail it advances forward till eventually it disappears; in older people, however, it may remain visible for a long time.

The circulatory system presents important symptoms, especially from a prognostic point of view. As in other febrile infectious diseases, the continued high temperature, the toxic products of the micro-organism, and the presence of the typhoid bacilli in the myocardium (Chantemesse), and especially also secondary infection, exert a deleterious effect on the heart muscle, and are often the cause of death in typhoid; the blood itself presents important changes which differ somewhat from those seen in other acute febrile affections, and lead to further disturbances, especially noticed in the post-febrile period.

Pulse. — During the first week, and during the whole period of the fever in cases which are likely to end in recovery, the pulse, except in children, ranges from 86 to 100 in men, and from 100 to 120 in women; it is distinctly and markedly dicrotic, indicating a paresis of the arterial muscular coat and low blood pressure. The force of the pulse varies, of course, with the age and strength of the individual and the condition of the heart; according to Potain, the blood pressure in the arteries is always diminished, see on this subject also Moser (65*a*). During the second and third week the pulse generally becomes a little quicker and less dicrotic, and during convalescence may be very slow. A small and quick pulse is of bad omen; Liebermeister found that when the pulse reached 140 pulsations per minute death occurred in 50 per cent, and when over 140 the mortality was 80 per cent. Equally unfavourable is the prognosis when the pulse becomes irregular and intermittent, even if not very frequent; such a pulse is often followed by pulmonary or cerebral thrombosis, with sudden death at a later period, and it indicates myocarditic changes. In some cases of enteric fever a slow pulse (50–40) has been noticed throughout the disease, which returned to its normal frequency during convalescence (Murchison). There is no definite relation between the temperature and the pulse, though often with rise of temperature the pulse also increases. The physical examination of the heart in ordinary uncomplicated cases reveals nothing abnormal; in severe cases the first sound may be very feeble or quite inaudible, as pointed out by Stokes; or the first and second sound become very similar in timbre and duration; sometimes a systolic murmur is heard at the apex or over the area of the pulmonary artery. With these signs dilatation of the heart, cyanosis, and venous pulsation may be noted. French observers have described a cardiac form of enteric fever. These cases are characterised from the first by quick, small, and irregular pulse, a low temperature, pallor of the face and extremities, and retrosternal pain. The prognosis of these cases is always very grave, and death often occurs from collapse or syncope.

As further complications, especially during the last stage of and during convalescence from enteric, blocking of arteries and of veins

occurs, the latter being much more common. The affection of the arteries has been described by Landouzy and Siredey as an arteritis, of which they distinguish a parietal and an obliterating form. This affection, if it occur, is almost always met with during convalescence; it affects the large trunks, and is ushered in by fever and by pain over the affected artery, which can be felt as a cord-like mass; the pulse in the vessels below the obstruction is very much diminished, œdema appears in the peripheral part of the affected limb, and in some cases dry gangrene follows: the surface temperature of the affected part is most usually diminished. In a case reported by Sydney Phillips (69), in which blocking of the left common femoral artery took place, the surface temperature of the affected limb showed an increase of 5° F.

Thrombosis of veins is of much more frequent occurrence. It affects most commonly the left femoral vein, but may affect other veins, as of the upper extremity; it is ushered in by slight rise of temperature, severe local pain, often lasting several days, and marked swelling of the limb; occasionally several attacks of thrombosis may occur during convalescence. In one case under my own observation each attack was preceded by a rigor, very high temperature, very quick pulse, and profuse sweating. In the clot obstructing the vein micro-organisms have been found (Vaquez). The thrombosis may extend into other veins; it may lead to pyæmic symptoms, and sometimes it causes sudden death from pulmonary embolism. If by the thrombosis of the vein the adjacent artery be much compressed, or if clotting in the artery be associated with it, gangrene of the distal part of the limb ensues.

Infarcts of the spleen, kidney, and lungs are sometimes seen post-mortem. Unless these infarcts are very extensive, they cannot often be diagnosed during life.

The blood in enteric fever shows some marked changes. For the literature on this subject I must refer to the paper by W. S. Thayer in the *Hospital Reports of the Harvard University*, vol. iv. No. 21, p. 83. The older writers state that the clot obtained by blood letting in this fever shows, by an absence of the buffy coat, that the fibrin is diminished. The histological examination of the blood has not always given uniform results, but the majority of observers are agreed upon the following broad facts: — the number of red blood corpuscles, normal at first, falls gradually during the fever, but not to a very large extent; with the cessation of the fever the number falls still lower, and may fall to a very low degree (post-typhoid anæmia). The red blood corpuscles may undergo temporary changes in number during the fever; thus profuse diarrhœa may cause a temporary increase, hæmorrhage a decrease. The amount of hæmoglobin falls and rises with the number of the red blood cells. The leucocytes are stated by most recent observers to be not only not increased, but rather diminished in enteric fever — a marked difference between enteric fever and inflammatory affections and other infectious fevers. Some observers, however, have noticed a slight increase at the beginning of the attack. With convalescence the number gradually

returns to the normal. In post-typhoid anæmia certain changes in the relative proportion of the various forms of leucocytes have been noted by Thayer, namely, a great increase of the large mononuclear leucocytes, and a diminution of the multinuclear neutrophiles. Eichhorst found in one case large granular cells containing several red blood corpuscles. The specific gravity of the blood taken after the method of Schmelz shows considerable diversity. The glycogen of the blood has been found increased. Typhoid bacilli have repeatedly been found in blood drawn from the spleen by a syringe, but very rarely in blood drawn from the finger or a superficial vein, or from the roseolar eruption. Streptococci and staphylococci have been found in the blood in mixed infection [see "Mixed Infection," p. 832].

Respiratory System. — Epistaxis as an early symptom has already been mentioned. In severe cases of the so-called "hæmorrhagic typhoid" profuse epistaxis, hæmorrhages from the stomach, kidneys, and other organs, and cutaneous and subcutaneous hæmorrhages, have been observed at a late stage of the fever.

Laryngeal Affections. — The larynx is not unfrequently found affected in enteric fever. About the proportion of cases affected authors vary considerably. In many cases there are no subjective symptoms, and laryngoscopic examination only can reveal the nature and extent of the affection; in others the symptoms are dryness and tickling of the throat, hoarseness, cough; while some affections, like œdema and perichondritis, may give rise to alarming and sometimes quickly fatal symptoms. The various affections are —

1. Catarrhal Affection. — This, according to Landgraf, Lewin, and others, is a simple hyperæmia of the mucous membrane.

2. Ulcerations, which, according to some observers, are due to the typhoid bacillus, and may thus be looked upon as a typical form of typhoid, "laryngo-typhoid." These ulcerations are situated in the parts of the larynx provided with adenoid tissue, namely, the base of the epiglottis, the posterior wall of the larynx, especially the inner surface of the arytenoid cartilages, and the false vocal cords. These ulcers may be simple erosions and heal readily, or they may become necrotic and leave sharply-defined defects, or they may lead to extensive perichondritis and exfoliation of the cartilages. As yet typhoid bacilli have not been found in these ulcers, and some therefore look upon them as allied to the next class, namely,

3. Ulcerations due to an epithelial necrosis, and caused by streptococci and staphylococci (Eppinger, Landgraf). They appear at first in the form of yellowish spots, which break up into smaller masses. These masses slough and become detached, leaving more or less deep ulcers, which may lead to further changes.

4. True Diphtheritic Affection. — This is extremely rare, and but few undoubted cases (35) are recorded. In one case the diphtheritic membranes extended to the bronchi, and the soft palate was also affected.

5. Perichondritis with exfoliation of the cartilages, which may lead

to marked narrowing of the larynx, or in rare cases to subcutaneous emphysema of the neck, must be looked upon in nearly all cases as secondary to the ulceration. It is chiefly noticed during convalescence; it may lead to suppuration and extensive destruction, and to alarming symptoms of suffocation. In several cases small portions of cartilage have been coughed up, and recovery has taken place; in many tracheotomy is necessary, though this is not unfrequently followed by fatal results (62). Some authors (Dietrich, Richle) have looked upon the laryngeal ulcers in enteric fever as allied in their origin and nature to bed-sores, and due partly to pressure and partly to disturbance in the circulation and innervation of the parts; they have accordingly proposed for these ulcers the name of "decubitus ulcers."

Lastly, we have to notice paralysis of the vocal cords, which has occasionally been observed during convalescence, or some time after. In some cases it has been found due to pressure on the recurrent laryngeal nerve, either by enlarged glands or thickened pleura (Schrötter); in others it is probably the result of changes in the muscles or nerves due to the toxic effect of the poison. Thus in one case paralysis of the vocal cord was noticed with multiple peripheral neuritis.

For a more detailed account of the laryngeal affections see (52, 28).

Bronchitis is very often noticed in enteric fever, especially in the older subjects. It may occasionally become very severe, and extend to the smallest bronchi.

Broncho-pneumonia occurs chiefly in the disseminated form, and may lead to small foci of suppuration.

Hypostatic congestion occurs frequently in enteric fever owing to the enforced and prolonged recumbent posture of the patient; it may lead to hypostatic pneumonia or collapse.

Croupous or Lobar Pneumonia. — It has now been clearly demonstrated that in most cases the pneumococcus of Fränkel is the cause of pneumonia in typhoid. In others (septic pneumonia) a streptococcus has been found. Some few cases are, however, recorded where the typhoid bacillus has been detected in the inflamed lung, and such cases must be regarded as a specific localisation of the disease (pneumotyphoid) (70*a*). Clinically considered, it must be noted that in some cases pneumonia occurs at the outset of the disease, and masks the enteric symptoms for some days, till in the second week, on the subsidence of the pneumonic symptoms, but slight abatement of the fever follows, and the enteric symptoms become more pronounced; in others, and this is more frequent, pneumonia sets in at the end of the second or third week of the fever. The usual symptoms — such as rigor, pain, and rusty sputum — are often absent, and the affection is often to be recognised only by increased frequency of breathing, by rise of temperature, and by the physical signs; in some few cases, however, acute pleuritic pain and rusty sputum may be noticed. Of the combination of septic pneumonia and enteric fever I have lately seen a case in which the pneumonia was of the creeping kind, attacking first the base and then the apex on each

side; the sputum contained masses of streptococci but no pneumococci. During the influenza epidemic the combination of influenza pneumonia with enteric fever was occasionally noticed (93). The association of pneumonia with true enteric fever must be distinguished from the "typhoid pneumonia," in which diarrhœa and all the symptoms known as the "typhoid" state occur — namely, great prostration, low muttering delirium, etc. In many cases the diagnosis cannot be made until the disease has lasted some days by the marked enlargement of the spleen, the appearance of roseolar spots, the persistence of the fever and the occurrence of intestinal hæmorrhage.

Pleurisy and empyema have occasionally been noticed during the course of enteric. Milder attacks of pleurisy, in which spontaneous absorption of exudation takes place, are not uncommon. Extensive exudations occur much less frequently, and are to be considered as the result of a mixed infection, due to streptococci or pneumococci. The typhoid bacillus has been found in a very few cases only (Weintrand, Belfanti).

Tuberculosis of the lung has occasionally been observed during convalescence or some time after; probably the disease in these cases was already present in the patient before he caught typhoid. Acute tuberculosis following enteric fever has been noted especially in some of the epidemics of enteric in soldiers during war (38).

The Mouth. — The state of the tongue, as already indicated in the general description, varies with the severity of the disease and the stage of the disease. At the onset it is covered with a white fur, which gradually thickens, but is still moist; and in milder cases this condition may not alter throughout the whole of the course: in the ordinary cases after the first week the tongue becomes dry, and is covered by a brown fur; later the dryness still further increases, and the centre of the tongue is covered by a deep brown, almost black, dry fur, which may form crusts and leave fissures. The gums and lips become likewise covered by brown, dry masses of sordes. With the beginning of convalescence the tongue becomes moist again and quickly cleans. The secretion of saliva is in most cases very much diminished, as indeed is the case in most fevers.

Parotitis is occasionally observed during the later course or as a sequela; it gives rise to more or less extensive swelling, and is usually unilateral; the exudation may gradually become absorbed, or suppuration may ensue, which not unfrequently leads to other septic symptoms and death. It is more frequently noticed in some epidemics than in others, and is either due to an extension of the inflammation from Steno's duct or to a metastatic inflammation. Murchison recorded six cases of which five terminated fatally; Osler noticed some cases which, however, all terminated favourably.

Cancrum oris occurs chiefly in children, and appears to be much less frequent now than formerly. It is observed during the latter stage of enteric, and its commencement, as it begins without pain as a small necrotic

patch on the mucous surface of the cheek, is not likely to be noticed. The necrotic patch extends in depth, and soon a hard, brawny, shining, indurated patch, at first pale and gradually deepening in colour, appears on the outside of the cheek; the patch softens, a deep slough forms, and on separation a hole may form through which the gums and teeth can be seen; at the same time the process extends on the mucous surface, causing extensive ulcerations of the gums, and even of the tongue. The gangrene may now spread farther, affecting the greater part of the cheek, the jaw may be laid bare, the teeth become loosened and fall out, and necrosis of the alveoli follow. There is marked salivation, and the breath is very fœtid. In spite of the extensive spreading of the necrosis there is rarely any hæmorrhage, and there is no pain throughout the whole course of the disease. In most cases the patient dies from septic pneumonia or other septic complication. Recovery is very rare, and in this event a marked disfiguration of the face remains. The affection is of the nature of gangrene, and is not due to typhoid bacilli; long threads of small bacilli have been found in the spreading edge by Lingard.

Pharynx. — Catarrhal affection of the pharynx is often observed, and during the latter stage of severe cases there is occasionally a thick deposit on the fauces, which can be detached, and is found to consist of débris, particles of food, masses of epithelial cells, leucocytes, and numerous micro-organisms. In some cases a deposit roughly resembling a diphtheritic membrane is seen; this owes its origin probably to streptococci and staphylococci, which are found in large numbers together with necrotic tissue and fibrin. This is usually a complication of very severe and fatal cases.

A peculiar ulceration has been described by several French and German observers (Bouveret, Devignac, Duguet, Wagner, Cahn) (9), and is looked upon as specific of enteric fever. It has been named pharyngo-typhoid. The ulcers are superficial, circumscribed, cleanly cut, and occur principally on the soft palate, close to the hard palate. From the observations of Rénon it appears, however, that they are not due to typhoid bacilli, but to streptococci and staphylococci.

Gastro-Intestinal Symptoms. — Nausea and vomiting, as already noticed, may be present at the onset and continue for some days. In most cases these symptoms disappear after the first week, so that the patient, as a rule, has no difficulty in taking large quantities of milk; the secretion of gastric juice is very much diminished, and free hydrochloric acid, as in most febrile affections, is absent. In cases where severe nephritis is noticed during the course of the fever, persistent vomiting, probably uræmic, has been noted. Epigastric pain and vomiting, due to inflammatory changes and ulceration of the stomach, have also been recorded (A. Chauffaro).

Diarrhœa is one of the characteristic symptoms of enteric fever. It may be present from the first, and persist throughout the whole course, continuing sometimes even when the temperature has reached the normal. In other cases there is constipation at first, and diarrhœa

begins about the end of first week; in others diarrhœa may be absent throughout, and even obstinate constipation may exist. Profuse diarrhœa is noticed principally in severe cases, but there is no relation between the diarrhœa and the ulceration of the intestines, and even in constipated patients extensive ulcerations have been found. The number of stools, usually four to ten in twenty-four hours, varies considerably; sometimes, however, the stools occur even more frequently. With each evacuation a fairly large quantity is discharged. The stool is thin at first, but of ordinary brown colour; soon it becomes yellowish, of the colour and consistency of pea-soup: it is often uniform, but in children, and sometimes in adults when very large quantities of milk are taken, it contains curds. With the approach of convalescence I have frequently noticed the colour of the stool to become greenish and less uniform, showing small solid particles. The stool, especially in children, has a very foul smell. On standing, a clear upper stratum separates, which is very rich in albumin. Microscopically examined the stool, besides the partly digested particles of food, contains a large quantity of triple phosphates, desquamated epithelial cells, embryonic cells, blood corpuscles, necrotic tissue elements, and granular detritus. Numerous micro-organisms are found, micrococci and larger and smaller bacilli. The typhoid bacillus has not been found in the alvine discharges before the ninth day; its detection, especially its distinction from the bacterium coli which occurs constantly in the fæces, both in health and in disease, has already been described; and it has been seen that at present no clinical diagnosis can be based upon it. Careful examination of the stool on the third week often reveals the presence of small shreds, probably sloughs from Peyer's patches. There is usually no pain either before or after the discharge.

Hæmorrhage from the bowels in any marked quantity occurs in from 3 to 7 per cent of the cases (Murchison, Liebermeister). It is much rarer in children. In some cases it may occur at the end of the first week, and is then probably due to intense congestion: most commonly it occurs after the second week; it may occur only once, and is then not a very unfavourable symptom, or repeatedly, and there may be eight to ten, and even more discharges in twenty-four hours, consisting of almost pure liquid blood. In two very severe cases (husband and wife) the hæmorrhage was so profuse that pressure on the abdomen, or any movement on the part of the patient, was followed by a discharge of blood, but both patients recovered. In less severe cases the stool is black and tarry. Slight hæmorrhage does not give rise to any subjective symptoms. Profuse hæmorrhage is indicated by a sensation of faintness, rapid fall of temperature (from 2° to 5° F.), pallor of the face, smallness and rapidity of the pulse, and extreme prostration. According to Zülzer, whose statement is confirmed by Moore, profuse hæmorrhage, by filling several coils of intestines, may give rise to a dull percussion note where previously the note was tympanitic. Such abundant hæmorrhage during the later stage of typhoid is due either to erosion of the vessels on the separation of a slough, or to an increased diapedesis from

the small arteries, whose walls are degenerated (72). As to the prognostic importance of the hæmorrhage authors differ somewhat. Graves, Trousseau, and Griesinger are of opinion that the occurrence of hæmorrhage is not an unfavourable symptom. This is probably correct when hæmorrhage occurs only once and early, as by the hæmorrhage some of the toxic material accumulating in the blood may be got rid of. Profuse hæmorrhage, on the other hand, occurring at a later period, must always be looked upon as a very serious event, and the mortality, from syncope chiefly, is very high (30 to 40 per cent).

In hæmorrhage typhoid, with petechial eruption, and abundant epistaxis, intestinal hæmorrhage is a prominent symptom, and may occur earlier in the disease.

Tympanites is almost a constant symptom in enteric fever, and when excessive is of grave omen. It may favour perforation, or by displacement of the diaphragm upwards cause cardiac disturbances. Of gurgling and pain on pressure we have already spoken. Abdominal tenderness is sometimes observed for the first week or later; it is sometimes diffuse, at other times limited to the region of the umbilicus, or the right iliac region. Persistent and localised pain is probably due to slight peritonitis.

Perforation of an intestinal ulcer is one of the most terrible of accidents. It seems to occur in about 2·5 to 3 per cent, and was noticed 114 times in 2000 fatal cases (42). It is rarer in children, and occurs more frequently in men than in women. It may occur any time after the second week, and it has been observed after all fever symptoms have subsided. Osler observed one case as early as the eighth day. In Hoelscher's table, of the 114 fatal cases, no case is recorded in the first two weeks of the fever. As accessory causes, indigestible food, excessive tympanites, obstinate vomiting, movements on the part of the patient, and the presence of intestinal worms, are cited; but occasionally perforation may occur without any such aids. It may occur in mild cases, and I have noticed it in apyrexial typhoid. The perforation, setting in suddenly, quickly gives rise to the symptoms of perforative peritonitis: severe pain, at first situated over the right iliac fossa (or referred pain over the left iliac region), soon becomes general. The pain may be persistent, or more like colic; in some few cases it has been entirely absent. Vomiting usually occurs early; the patient shows symptoms of collapse; the features become pale and pinched, the pulse small and threadlike, the abdomen more distended, and the liver dulness can no longer be made out on percussion (Wagner, Flint). In some cases the abdomen, instead of being distended, may be retracted, with marked rigidity of the walls (Wagner). The breathing becomes thoracic, and the temperature suddenly falls, though it may afterwards rise again considerably. There is often suppression of urine. Soon the prostration becomes extreme, the voice husky, cold clammy perspiration covers the face and body, and the patient gradually sinks, the sensorium often remaining clear to the end. In some cases death may occur at a later

period from subacute peritonitis. Thus a patient was admitted into the Manchester Infirmary with symptoms of intestinal obstruction which had lasted for some days; the patient died soon after admission. At the autopsy typical typhoid ulcers were found, one of which was perforated, and fæcal extravasation had taken place. There was extensive peritonitis and a small quantity of fæcal matter lay free in the abdomen. Recovery does occasionally, but very rarely, occur. If the perforation be a tiny one the symptoms may not be very characteristic: the pulse, however, will rise over 120, and the temperature may fall. The area of liver dulness may also be diminished, and the respiration be thoracic. There may be a disposition to vomit, and a little increasing pain. Yet even in such a case laparotomy can scarcely be advisable, as the enfeebled heart, extensive intestinal ulceration, and febrile prostration, prevent much hope of success.

Perforative peritonitis, apart from the perforation of an ulcer, may occur from ulceration of the gall-bladder, rupture of a suppurating mesenteric gland or of abscess of spleen, rupture of spleen, etc.

The occurrence of peritonitis without perforation may occur from extension of the inflammation to the serous coat of the intestine. It is then generally circumscribed, and tends to form adhesions. Occasionally it may give rise to a local suppuration.

Complications relating to the Liver and Biliary Apparatus. — Recent experimental investigations have shown that in microbic diseases the liver plays an important part, the vessels with their endothelial lining, and probably also the liver cells, being actively concerned; but these changes do not give rise to symptoms which can be clinically recognised, and the changes which we notice are due not so much to the typhoid bacillus, as to a mixed or secondary infection, and to complications.

Jaundice is very rare in the enteric fever of our climate. It has been noticed late in the disease, or even during convalescence, and is most commonly due to catarrhal secretions blocking up the bile duct. In other cases the jaundice is due to micro-organisms which have been found in the biliary passages, such as the bacterium coli commune, streptococcus pyogenes, etc., which give rise to inflammation of the biliary ducts (cholangitis) with or without formation of abscesses. Such cases usually run a fatal course, with symptoms of pyæmia. The gall-bladder from a similar cause may be the seat of suppuration, and may even be ruptured. Some observers draw attention to the formation of gall-stones after recovery from enteric fever, and Dufourt collected nineteen cases where gall-stone colic occurred thereafter. Chantemesse gives a case where a woman eight months after enteric began to suffer from hepatic colic, jaundice, and fever. The gall-bladder, removed by operation during life, showed the presence of biliary catarrh and living typhoid bacilli. I may here draw attention to the not unfrequent coexistence of gall-stone and ulcerative endocarditis [see article on "Ulcerative Endocarditis"].

Spleen. — The enlargement of the spleen is a constant symptom in enteric fever, and its gradual increase can often be demonstrated during

the course of the disease. During the second week, especially in children, the edge of the spleen can often be readily felt, particularly on deep inspiration. The enlargement continues to the end of the third week, when it gradually subsides. The spleen is found increased in its various dimensions, and the enlargement can be readily made out by percussion. When there is great distension of the abdomen, or when the stomach or colon are inflated and displaced, the splenic enlargement cannot easily be made out; in other cases the area of splenic dulness, though not enlarged, is increased in intensity. Palpation of the spleen is occasionally painful. Abscesses and rupture of the spleen have been occasionally noticed; they are, however, extremely rare, and more of pathological than clinical interest.

Genito-Urinary System. — The urine in enteric fever presents the ordinary character of febrine urine. It is decreased in quantity, high-coloured, very acid, and of high specific gravity. Uric acid, kreatinin, and ammonia are increased; urea is usually increased, though sometimes it is diminished during the first few days. Chloride of sodium[1] and phosphoric acid (Zuelzer) are found diminished — the potash salts and relative sulphuric acid (Zuelzer) increased. Of abnormal constituents, albumin is found in 70–80 per cent of the more severe cases. Of the various forms of albumin serumalbumin is constantly found, and with serumalbumin globulin often, hemi-albuminose or prepeptone occasionally. In several cases the urine has given the reactions of hemi-albuminose for one or two days, which was then replaced by serumalbumin. The urine may contain blood when hæmorrhagic nephritis complicates enteric fever, and in petechial typhoid. In some severe cases hæmoglobinuria has been observed. Mucus occurs when cystitis is present. In some cases acetone and aceto-acetic acid are found in the urine without the presence of sugar. Microscopic examination may reveal the presence of various forms of casts, as will be presently pointed out. In very severe cases of enteric fever leucin and tyrosin have been found in the urine.

Ehrlich's Diazo Reaction. — Ehrlich described this test in 1882, and since then a large number of observations have appeared on the subject (40). The peculiar reaction is probably due to the presence of some nitrogenous products in the urine. To carry out the test we use two solutions: No. 1, a saturated solution of sulphanilic acid in dilute hydrochloric acid (1 in 20); No. 2, a solution of sodium nitrite in water ($\frac{1}{2}$ per cent solution). The urine to be tested is put into a test-tube, and a quantity of the solutions 1 and 2 equal to that of the urine is added (about 40 c.c. of the sulphanilic acid and 1 c.c. of sodium nitrite solution), the mixture is well shaken, and then some drops of liquor ammoniæ are allowed to slip down the side of the tube. At the junction of the two a deep brownish red ring appears; if again shaken the whole

[1] Terray (88) compared the quantity of sodium chloride in the food with that voided by the urine and the fæces in four cases of enteric fever, and found the chloride diminish during the whole fever period, and also for some days after the fever had disappeared. The diminution, according to Leyden, is due to the retention of water in the system during the fever.

fluid mass appears red, and if the diazo reaction be present the foam appears also rose tinted. This test has undoubtedly some diagnostic value (87). It is certainly present in a very large majority of cases of enteric fever both in adults and in children, and even in the apyrexial type; according to Taylor, it does not often appear before the end of the first week (Hewetson noticed it in 77 per cent of his cases in the first week), and it often disappears during the third and fourth week. The reaction, however, is also seen in other febrile affections (typhus, measles, scarlet fever, pneumonia, acute tuberculosis), and in some apyrexial diseases (chronic hepatitis, carcinoma, leukæmia, etc.), and its diagnostic value is thereby somewhat lessened.

Albumin in the urine is an important symptom; it is not always due to the same cause, and from analogy with other infectious diseases, and from a consideration of the pathological changes in the kidney found after death, we may distinguish the following forms of albuminuria: —

1. Febrile Albuminuria. — The albuminuria is here due to the pyrexia,[1] though the retention of toxic products in the blood cannot be overlooked as a probable cause. Clinically this albuminuria is characterised by the small amount of albumin in the urine without blood, and often without casts; if casts be present they are hyaline and few in number. This albuminuria may be noted early, sometimes even in the first week. It occurs in children as well as in adults; it is sometimes absent for a day or two, and it disappears with convalescence. It does not give rise to very serious symptoms, and is not followed by any permanent damage of the kidney.

2. Albuminuria due to Acute Bright's Disease (Hæmorrhagic Nephritis, Nephro-typhoid). — The albumin is here often abundant; the urine contains also blood, and granular, fatty, and blood casts are seen. Various micro-organisms, amongst them the typhoid bacilli, have been found occasionally in the urine during life, or in the kidneys after death in this affection. This complication, if stress be laid on the free admixture of blood, is of rare occurrence — the presence of large quantities of albumin and casts without any blood, or with but a small quantity of blood, is of more frequent occurrence (Osler and Mason's figures give about 10 per cent of the observed cases of enteric fever). This complication is usually observed in the second week, but sometimes (Gubler, Robin) it may be an early symptom. It may last for several days, and end in recovery; or uræmic symptoms, low delirium and convulsions may set in. When this complication occurs early with pain in the back and the passage of urine containing much blood, and is followed by uræmic symptoms, the primary disease is difficult to recognise. The affection is most likely due to the action of bacterial products on the kidney, products which either circulate in the blood or pass to the kidney from another

[1] As it has been demonstrated by means of Roy's oakometer that with an increase of the body temperature the kidneys decrease in size considerably, the diminished quantity of urine passed and the presence of albumin in the urine are readily explained (64); again experimental investigations have shown that albumin may appear in the urine of animals exposed to high temperatures.

part of the urinary tract (67): thus it is allied to the nephritis seen in other infectious fevers, and scarcely deserves the designation of nephro-typhoid.

3. As septic infection is a common complication of enteric fever, we notice sometimes an acute suppurative nephritis, an earlier stage of what is probably Wagner's lymphatic nephritis. This gives rise to no diagnostic symptoms, except perhaps the presence of multinuclear leucocytes in the urine not due to any other complication in the urinary tracts, such as cystitis.

4. During convalescence albuminuria may be observed with other symptoms of nephritis, and be followed by œdema. It is allied to the post-febrile nephritis seen in other infectious fevers (Osler).

Of other complications we may notice: —

Pyelitis, cystitis, when there has been retention of urine, *hæmorrhage from the bladder, urethritis.*

Orchitis, followed by epididymitis, occurs during convalescence. The patient becomes again feverish, the testicle is very painful and swells rapidly. Resolution sets in quickly, or suppuration ensues.

Ovaritis and *salpingitis* have also been occasionally noticed. Changes in the menstrual period occur sometimes during convalescence.

Symptoms relating to the Nervous System. — The nervous system is often profoundly implicated in enteric fever throughout the fever period and even after; so much so that in Germany the popular designation of typhoid is nervous fever (*Nervenfieber*). The nervous symptoms vary considerably in individual cases.

At the onset, and sometimes even during the incubation period, headache and insomnia are the principal features; these usually subside after the first week. In milder cases there may be no other symptoms within the nervous sphere; in the more severe cases there are symptoms of irritation, and in the most severe cases of paralysis of the higher centres. Some of these have already been alluded to in the general description of the disease.

Delirium is common in the ordinary, and especially in the severer cases. In the milder cases it may only occur at night, when the patient awakes from a slight slumber; in the more severe cases it is persistent, but varies in its manifestations. We have the quiet delirium, when the patient is easily roused, answers questions fairly rationally, but soon lapses into delirium again: violent delirium, when the patient gets very excited, talks or sings, or may even become violent; this may lead gradually to acute maniacal delirium, which sometimes occurs in paroxysms, during which the patient must be carefully watched, as he may attempt to escape or do himself some bodily injury. It must be remembered that even without showing marked signs of delirium patients in enteric fever may manifest suicidal tendencies. Low muttering delirium is seen in the more severe cases: the patient is restless, mutters constantly, and trembles and twitches; equally serious is the delirium in which the patient is quiet, lies with his eyes open, but is quite uncon-

scious. The more severe forms often lead to coma. In tipplers the delirium often takes the form of delirium tremens — the patient converses with imaginary people, fancies himself at his usual avocations, gives orders, or serves customers, etc.

In some cases, especially in women, the delirium has more the character of lipemania; the patient imagines himself the subject of some persecution, he refuses to speak, keeps himself wrapped up in his blankets, appears terrified when any one approaches him, and is often absorbed in one fixed idea (4). The fixed idea from which the fever patient suffers sometimes persists for a while during convalescence. In one case a patient fancied he had received a commission in Her Majesty's service, and after he recovered from the fever he searched over all the newspapers to see if he had not been gazetted.

In most cases the delirium occurs during or after the second week, but occasionally it is an early symptom, and when preceded by headache, and accompanied, as it sometimes is, by retraction of the head and neck, convulsions, tâches cerebrales, etc., — and these occur more particularly in children, — the diagnosis from meningitis is often difficult; in some cases, indeed, the post-mortem examination has shown the existence of meningitis besides the lesions of enteric fever. The meningitis may be the result of a mixed infection; the typhoid bacillus, however, has been found in the meningeal exudation (Ferul).

Convulsions are noticed sometimes in children, both at the onset and during the course of the disease; in adults they occur sometimes in the meningeal form, or from uræmia in the so-called nephro-typhoid; or they may precede death when myocarditis complicates enteric fever. Severe nervous symptoms are seen, especially in those patients who have a marked neurotic disposition, either acquired or inherited; though the toxic effects of the fever poison cannot be excluded.

The deep reflexes (knee-jerks) have been found increased, but this, from numerous observations I have made, is not invariably the case. I have found the knee-jerks absent in a few cases, though there were no indications of peripheral neuritis; in this latter case the knee-jerks are absent.

The muscles often show increased irritability, and when marked emaciation is present they exhibit idiopathic contractions on being tapped. Muscular tremors affecting the limbs (the upper extremity more than the lower extremity), the tongue, and sometimes the muscles of the face, often accompany other severe nervous symptoms; and subsultus tendinum in enteric as well as in other affections is a grave though not a fatal omen.

Retraction of the head and rigidity of the muscles of the neck, back, or extremities, may occur in severe cases, and, if associated with comatose symptoms, may suggest epidemic cerebro-spinal meningitis.

There is scarcely any other febrile affection, except perhaps epidemic influenza, which is followed by so many nervous sequelæ as enteric fever. Some of these are observed during the decline of the fever and during convalescence, others occur some time after. Of these we may mention —

Mental Diseases. — Loss of memory and feebleness of intelligence, leading to dementia, melancholia, monomania, and other forms of insanity, may appear. Some of these symptoms, probably due to malnutrition, are of short duration; others, probably due to the toxic effect on the nerve elements, are of longer duration; in some cases recovery takes place after many months, whilst others remain incurable.

Aphasia has often been observed in children, and is generally a temporary affection.

Neurasthenia in its various forms may supervene — cerebro-spinal, spinal, sympathetic, and visceral. Under the name of "typhoid spine," cases of spinal neurasthenia, characterised by severe pain in the back and sometimes in the legs, have been described (67).

Local pain, allied to local neurasthenia (topalgia of Blocqui), is occasionally noticed. The affection described as tender toes (acroparæsthesia of Schulze), that is, an excessive tenderness on the slightest pressure of the toes, sole of the foot, and sometimes dorsal surface of the foot, also belong to this group; the opposite of this, more or less persistent anæsthesia of a circumscribed area, not due to peripheral neuritis, is occasionally seen. Local vaso-motor neurosis, consisting of redness with slight swelling of parts of the extremities, has been described.

Hysterical manifestations during convalescence are not frequent, yet are occasionally seen both in men and women.

Hemiplegia, due to hæmorrhage, thrombosis, or merely temporary and due to anæmia or spasm of the arteries, is very rare in enteric.

Disseminated sclerosis is found more often after enteric fever than after any other infectious disease.

Acute disseminated myelitis is mentioned by Leyden and others as following enteric fever (21).

Poliomyelitis. — Paralysis of one limb or portion of a limb, followed by atrophy, with partial recovery, has occasionally been noticed. Some of these cases are more likely to be forms of peripheral neuritis (80); some are due to an acute inflammation of the anterior cornua, as proved by the post-mortem examination (80).

A peculiar complication occurring in enteric fever has been described by Eisenlohr (24). In three cases he observed symptoms of bulbar paralysis, affecting the lips and tongue, interfering with articulation, and accompanied by weakness in the muscles of the trunk. One of the three cases ended fatally, and numerous typhoid bacilli were found in the brain, medulla, cord, and chiasma of optic nerves.

Peripheral Neuritis. — Occasionally extensive multiple neuritis, affecting both upper and lower extremities, with sensory disturbances and atrophy, is seen. One such case I saw in a young girl (75*a*), and the other in a child three years old, in whom contraction of both hands and feet set in after the paralysis had been established, but it yielded completely to treatment. More often the peripheral neuritis is located in a plexus of nerves, or in the root or trunk of one nerve only. The affection usually sets in with excessive pain, followed by numbness and

paresis, going on sometimes to complete paralysis of the muscles supplied by the affected nerve or nerves, and often followed by marked atrophy. I have seen one case in which the root (both sensory and motor) of the fifth was evidently affected; partial recovery took place. Prof. Osler has recently published some careful observations on such cases (67*a*).

Paralysis of cranial nerves is very rare in enteric fever. Occasionally paralysis of one or other of the ocular muscles has been noticed.

Of the special sense organs hearing is commonly affected in enteric fever. In many cases the deafness is due to otitis media, which in the course of time may be followed by the well-known cerebral complications — meningitis, thrombosis of cerebral sinus, abscess of the brain. Sometimes the deafness is due to an affection of the auditory nerve, and is more permanent.

Optic neuritis is a rare complication. I have seen one case in which amblyopia and colour blindness occurred in one eye after the fever, and the optic disk was blurred; this probably was a case of retrobulbar neuritis. Ulceration of the cornea and suppuration of the orbit have been described (Panas).

Bone and Joint Affections. — It has been pointed out by Chantemesse, that in inoculation experiments the typhoid bacillus can be traced to the medulla of bone, and it is therefore not astonishing to find that affections of the bones are no uncommon sequelæ of enteric fever. The most common event is the formation of an abscess periosteal or myelogenic. The tibia and femur are the usual seats of these abscesses, though they may occur in other bones, such as the sternum, ribs, etc. In the pus of them streptococci or staphylococci have been found; in some, however, only the typhoid bacillus. These abscesses, ushered in by severe and persistent pains, redness, and swelling of the affected part, often occur many months after the fever; and, in a case recently recorded by Buschke, forty-six years had elapsed since the occurrence of enteric fever, yet the typhoid bacillus found in the pus was capable of further growth and cultivation. In other cases the bone, instead of undergoing suppuration, becomes hypertrophic and deformed — hypertrophic osteitis.

In children and young persons, after convalescence one occasionally notices an exaggerated growth of the bones. Sometimes a circumscribed periostitis is recorded, which comes on without any great pain, and may undergo complete absorption (Hutinel).

The joint affections associated with or following enteric fever vary in their nature.

1. Pain and swelling of one or more joints (the smaller joints, the ankle, wrist, and knee) is not a rare symptom in enteric fever, and may come on early in the disease. The symptoms generally subside during convalescence. As this is seen in pure and uncomplicated cases it is probably more or less directly connected with the typhoid poison itself (31).

2. The osteitis before described, when situated near the joint, may extend to the joint itself, and osteo-arthritis, with marked pain and swelling of the joint, and occasionally even suppuration, may occur.

3. Septic arthritis, usually with other pyæmic symptoms, is seen in the mixed infection.

4. Occasionally rheumatic arthritis, affecting several joints, may complicate and follow enteric fever, and set up endocarditis (94).

Of other complications we have only yet to mention —

Suppuration of the Thyroid Gland. — Golgi found the typhoid bacillus in the pus (17*a*).

The Nutrition of the Body in Enteric Fever. — Emaciation is most pronounced, especially during the latter part of the attack. According to Robin (75), a person suffering from enteric fever eliminates more solids (52 grammes) than a healthy, well-nourished person (50 grammes). This, apart from many other factors, would explain the emaciation. The daily loss of weight is about 238 grammes. Klemperer's observations further show that during the fever the food albumin is not completely used up by the patient, who therefore gives up part of his body albumin. Ziemec (102) found an average daily loss of body weight of 0·9 per cent during the fever, a figure much lower than Robin's.

[The subject of tissue metabolism in fever is set forth in the art. "Doctrine of Fever."]

Relapse. — I have already spoken of a recrudescence of the pyrexia during convalescence from various causes. From this the true relapse must be distinguished, which is indeed a fresh attack of enteric fever, and in it appear many of the noteworthy symptoms, such as tympanites, diarrhœa often with slight hæmorrhages, a second series of roseolar spots, a further enlargement of the spleen, and pyrexia with marked evening exacerbations. These symptoms, of course, are not all constantly present. In the presence of the eruption and the renewed pyrexia, and in the absence of any local inflammation, the diagnosis of a true relapse must be based.

Authors differ somewhat as to the frequency of relapse. Murchison's estimate is 3 per cent, Griesinger 6 per cent, whilst Shattuck gives over 16 per cent. Men appear more liable to it than women. The duration of the relapse varies from nine to twenty-one days; thus it is shorter, and as a rule the symptoms are less severe than in the primary attack. In Shattuck's twenty-one cases of relapse there was only one death.

The relapse may occur early or late during convalescence; in several cases I have seen it occur only a few days after defervescence; in most cases it occurs within the first fortnight of convalescence, whilst occasionally even a month or more may elapse before its occurrence.

The first relapse may be followed by a second, and sometimes even by a third and fourth relapse, but as a rule the subsequent attacks are shorter in duration and milder in their symptoms. The cause of the relapse is most likely a reabsorption of the poison, and probably glands which escaped the typhoid bacillus during the primary attack of fever become affected; or it may be that some of the poison is retained in the spleen or some other organ, and is subsequently liberated and thrown into the circulation.

Mixed Infection. — When describing the symptoms and complications of enteric fever I have repeatedly drawn attention to the presence of other micro-organisms found in the diseased tissue, which must be looked upon as the cause of these complications; and we know now that in many of these complications not only in enteric fever, but in other infectious diseases, both acute and chronic (pneumonia, diphtheria, scarlatina, tuberculosis, etc.), mixed infection plays an important part. It is well to distinguish between *double* infection and *secondary* infection. In the first case the symptoms of the two different diseases are present and can be readily distinguished, their association often being only a coincidence, as, for example, enteric fever and tuberculosis, or enteric fever and typical diphtheria due to Löffler's bacillus. The chief double infections which have been noticed in enteric fever are with tuberculosis — coming on chiefly after convalescence — scarlet fever, diphtheria, cholera, anthrax, erysipelas, and malaria. In the second case, the *secondary* infection, the presence of one organism favours the development of the other. Thus it is now well established that the tubercle bacillus favours the growth and development of the streptococcus; many of the lesions and symptoms of phthisis are due to the latter and not to the former micro-organism. The same holds good for enteric fever, as the typhoid bacillus favours the growth of other micro-organisms, such as the streptococcus, the staphylococcus pyogenes, the bacterium coli, and the pneumococcus. There are various circumstances which may explain the development of these secondary micro-organisms, most of which may occur in the human body or its surroundings; as for example the weakened state of the system, the ulcerated condition of the intestines and other organs giving free access to the micro-organisms to the system, the presence of toxins in the blood, etc. The most common secondary infection is of septic nature, and due to the various pathogenetic cocci. It is not always easy to distinguish the septic complications from the changes due to the typhoid bacillus itself, especially as it has been shown that the typhoid bacillus has pyogenetic properties, and may induce suppuration (71, 36, 7). Bacterioscopic examination of the blood will enable us sometimes to detect the pathogenetic cocci in the blood of the typhoid patient (83). Want of attention to the proper hygienic measures may easily lead to secondary infection. An instance in point is an observation by Korczynski and Gluzinski (48), in a ward previously occupied by many surgical cases wherein a number of patients affected with enteric fever were afterwards placed. Great mortality from septicæmia, pyæmia, phlegmonous inflammations, etc., ensued, and dust from the ward showed the presence of staphylococcus aureus, and the streptococcus pyogenes citreus and albus. After thorough disinfection of the ward these septic complications disappeared to a great extent. Cases of measles and of other acute infectious fevers in these wards showed no such complications.

Varieties of Enteric Fever. — The diversity in the symptoms and course of enteric fever has led authors to distinguish certain varieties of enteric

fever. The usual classification, one which recommends itself from a clinical and practical point of view, is the following: —

1. The Abortive Form. — The disease begins, like an ordinary attack of enteric fever, with high temperature, repeated shivers, enlargement of the spleen, diarrhœa and roseola, or some of these. Early in the second week the fever falls, and by the end of the week there may be complete defervescence. Relapses have been noticed.

2. The Mild Form. — The symptoms are slight throughout the course of the disease, which lasts from sixteen to twenty-one days: the temperature does not reach 103°; diarrhœa, if present, is mild; the prostration not great. There is no great emaciation, and convalescence is usually rapid.

3. Ambulatory Typhoid (walking typhoid, or latent typhoid). — The symptoms are here so slight that the patient follows his work, though more or less troubled with loss of appetite, diarrhœa and headache. Patients suffering from this form have often been known to walk to the out patients' room, where by the condition of the tongue, the tremor, and the temperature, the true nature of the case is recognised. In other cases violent delirium or profuse intestinal hæmorrhage is the first symptom which brings the patient to the doctor; and if death occur soon after, as it often does, extensive intestinal ulcerations are found; or sudden death may occur from perforation (92). I remember one case of a workman who, whilst repairing the roof of a house, fell off and was killed by the fall; at the post-mortem examination, besides fracture of the skull, there were found typical typhoid ulcers in the ileum. At the inquest the wife of the deceased stated that her husband had complained of headache, lassitude, and giddiness for some days.

4. The apyrexial form, which runs its course without any perceptible pyrexia.

5. The grave form of enteric fever, characterised by high fever and grave nervous symptoms. According to the more prominent symptoms we distinguish under this head — (*a*) The Bilious Form (fièvre bilieuse). Frequent and persistent vomiting of bilious matter, with severe and persistent headache; pulse quick and small; the case often ends fatally about the end of the second week from asthenia; delirium generally absent. (*b*) The Ataxic Form. — Delirium with hallucinations prominent, typhoid symptoms severe, and sometimes convulsions occur. (*c*) The Adynamic Form. — From the outset there are great prostration, very weak heart's action, abundant diarrhœa, low delirium, profound stupor: if these symptoms are associated with subcutaneous and internal hæmorrhages the case is spoken of as the hæmorrhagic form.

Most of these severe forms are due to a secondary infection of septic nature. Pharyngo-typhoid, laryngo-typhoid, pneumo-typhoid, nephro-typhoid, cardio-typhoid, are often instances of mixed infection, as already mentioned.

6. Spleno-typhoid occupies a somewhat different position. It is characterised clinically by a type of fever which in the excessive enlarge-

ment of the spleen, and in the absence of intestinal symptoms, rather resembles that of relapsing fever (though spirilla are not found in the blood). The lesions in Peyer's patches are not well developed, only congestion and swelling being noticed (23). Moore (65) observed a case in which Peyer's patches were not even hyperæmic.

7. Enteric fever in children is not rare. Some of the peculiarities observed in infantile enteric fever we have already noticed. In some cases the infection runs the same course as in the adult, in others the fever has a remittent type (infantile remittent fever), the evening temperature being 2° to 3° higher than the morning temperature. Abortive enteric fever is also noticed, likewise the bilious form. A respiratory or thoracic type has been described by some, the more prominent symptoms being quickened respiration, marked dyspnœa and cyanosis, and the presence of fine râles over one or both lungs. A meningeal type may be distinguished which sets in with headache, vomiting, and convulsions, and is followed by delirium, great prostration, and torpor. Diarrhœa and involuntary discharge of fæces is not infrequent, and the diagnosis from meningitis is often difficult. In these cases strabismus, inequality of pupils, injection of the conjunctivæ, and even the hydrocephalic cry (8), may occur. Finally, a spinal type, with hyperæsthesia of the skin, contraction of muscles and opisthotonus (26), is also described.

8. Enteric Fever in the Aged. — Enteric fever is not common in persons after forty; but in epidemics old people are not infrequently affected. I have seen a typical case of typhoid in a man seventy-five years old.[1] The affection usually commences insidiously with headache, loss of appetite, epistaxis; the fever is not very high, and rarely reaches 103°; diarrhœa is present, but not usually profuse. Death sometimes takes place before the end of the third week from pulmonary œdema or failure of the heart. The mortality is high.

9. Malario-typhoid. — See articles on Malaria and on Climate and Fevers of India.

10. An epidemic atypical form of enteric fever, occurring only in those who shortly before had suffered from malaria, is described by Karlinski (45). It was observed in Bosnia, and called there dog-typhoid (*Hunde-typhus*). (The typhoid bacillus was found in the fæces in these cases.)

Diagnosis. — The diagnosis of enteric fever is often made without difficulty; sometimes the diagnosis can only be made after watching the symptoms for some days, whilst in not a few cases it is impossible to arrive at a definite diagnosis. It is during the first week of the fever that the difficulty of diagnosing the disease is so great, and here Wunderlich's propositions as to the temperature will be found a very useful guide; also such symptoms as severe headache, sleeplessness, epistaxis. Ehrlich's diazo reaction, though present in most cases, is also noticed in

[1] A well-marked and severe case occurred many years ago under my care in a vigorous old gentleman of eighty-two. By the labours of six nurses, working in pairs for eight hour watches, he was brought to recovery, but only to die during convalescence of a diaphragmatic hernia. — Ed.

other febrile affections, and being often absent during the first week, is of no great help in doubtful cases. Nor as yet can the detection of the typhoid bacilli in the stools be made of use for clinical purposes, as their isolation and distinction from the bacterium coli take much time, and are processes too elaborate to be clinically useful: moreover the bacilli have not been found in the stool before the eighth or ninth day of the fever. The same applies to the detection of the bacilli in the urine, though, according to some observers, they may be found earlier, which seems to me very doubtful; and in the blood, where they have only been found very rarely: we cannot countenance puncture of the spleen for the detection of the typhoid bacilli. In distinguishing enteric fever from other affections we must note the temperature curves, the intestinal symptoms, the characteristic rash, the enlarged spleen, and other less prominent symptoms. Thus, in *typhus* fever we have the typhoid state, and we may have diarrhœa, but the fever is less gradual in onset; it remains high during the whole time of the fever, and on the fourteenth day there is usually a crisis and a rapid fall to the normal.[1] The rash in typhus appears earlier, generally about the fourth day, does not occur in successive crops, and persists to the end of the fever; the rash consists of spots of irregular form, red or dirty pink, which become reddish brown and then do not disappear on pressure, they often become hæmorrhagic, and they are more numerous and more widely distributed; besides the spots there is marked mottling of the skin of the abdomen. Violent delirium is much rarer in typhus than in enteric fever.

In *tubercular meningitis* the temperature is rarely so high as in enteric fever with marked cerebral symptoms; the pulse if soft is no longer dicrotic, and may even be hard; persistent vomiting during the first few days occurs more frequently, and the abdomen is generally retracted. Optic neuritis, whilst extremely rare in enteric fever, is not uncommon in meningitis; the same may be said of the inequality of pupils, and of squint. Tubercle of the choroid would be, of course, a pathognomonic sign, but it is not often present in the latter disease.

In *acute general miliary tuberculosis* we may have the history of previous cough or pleurisy; the temperature is not so high, the pulse is not dicrotic, the abdomen is retracted, roseola is rare, the examination of the stools may sometimes show the presence of tubercle bacilli, and emaciation is noticed early in the disease; yet in some cases the diagnosis is impossible. A roseolar rash may occur, though very rarely, in miliary tuberculosis; I have seen it in three cases — two at the Fever Hospital, and one under the care of my colleague, Dr. Steell, at the Manchester Infirmary. Diarrhœa and even intestinal hæmorrhage may be noticed, with tympanites and gurgling in the right iliac fossa, while the temperature curve may be very much like that of enteric fever (79).

[1] It is generally stated that in typhus the fever terminates abruptly in a crisis. According to Dr. Steell's observations (83*a*) this is not correct; the defervescence is gradual, lasting two days, and the fall of the pulse during the period of defervescence is also gradual.

The much quicker pulse and the absence of dicrotism appear to me to be very significant distinguishing features in acute miliary tuberculosis, and also the aspect which is usually alert and even excited; not oppressed, not apathetic, save towards the end; rarely even indifferent.

Tubercular peritonitis may simulate enteric fever. I recall two cases admitted into the Monsall Hospital as enteric fever, in which for several weeks the symptoms much resembled it. In one of the two cases large tumour masses in the abdomen could be detected about the fourth week of illness, and in the other case, after some weeks of pyrexia, fluid was discovered in the abdomen; in both cases the pulse was over 130 for many days.

The gastro-intestinal form of epidemic influenza may closely simulate enteric fever. We may have a roseolar rash (though this is very rare, and when it does occur is more widely distributed, and does not appear in successive crops), tympanites, gurgling (which, however, is not confined to the right iliac fossa), a markedly enlarged spleen, and profuse diarrhœa. The sudden onset of the fever, which often in less than twenty-four hours reaches 103° and 104°, and the subsidence of the fever symptoms before the end of the second week, will help us to distinguish influenza from enteric fever, so will also the condition of the tongue and pulse. In some cases of influenza the pyrexia persists for several weeks, but diarrhœa and the other symptoms have then subsided (57). If there be cough with expectoration, the examination of the sputum for influenza bacilli, which can be easily recognised without any cultivation, will assist us materially to a correct diagnosis. I must, however, here observe that enteric fever and influenza may occur together. I have seen two undoubted cases of enteric fever immediately following an attack of epidemic influenza: in one the diagnosis was verified by a post-mortem examination, and in the second there was a distinct relapse after the enteric fever. Both cases occurred in adults; several members of the family were affected with typical influenza at the time, and in both cases a subsidence of the influenza symptoms had taken place, when the temperature again rose, and gradually all the prominent symptoms of enteric fever were manifested.

We have already spoken of *pneumonia complicating typhoid*, and of *typhoid pneumonia*. There is, however, a form of pneumonia — the *cerebral pneumonia* — where the symptoms for a few days very much resemble those of enteric fever. There may be no rigor, no pleuritic pain, the onset of the fever may not be sudden, and on physical examination of the chest no signs of pneumonia may be noticed for several days, that is to say, until the pneumonic process has reached the periphery of the lung.

Pyæmic and septicæmic affections, such as *ulcerative endocarditis*, *osteomyelitis*, idiopathic *pyo-septicæmia*, and *puerperal septicæmia*, may produce a train of symptoms very much like those of enteric fever, including a roseolar rash, tumefaction of the spleen, and diarrhœal tympanites. Thus three members of one family had lived in a cellar dwelling, which had been under water at a time of an extensive flood, and being attacked with

febrile symptoms, they were sent to the Monsall Fever Hospital. Their symptoms closely resembled those of enteric fever, and one of them presented on the third day of admission marked roseolar spots, and had slight intestinal hæmorrhage on the fifth day; the temperature showed marked evening exacerbations; the patient died from exhaustion on the fourteenth day after admission (about the seventeenth day of the fever), and on post-mortem examination the intestines appeared healthy. I could quote several other similar cases. *Puerperal septicæmia* may sometimes be indistinguishable from enteric fever. Thus in a case reported by Leu (59), a roseolar rash, tympanites, enlarged spleen, intestinal hæmorrhage, and a pyrexial curve like that of enteric fever were noted. In most cases of puerperal septicæmia, however, we notice, apart from any local symptoms, a high temperature early in the disease. There is from the first and often throughout the course of the disease vomiting and profuse diarrhœa; the pulse from the first is quick, and not dicrotic; the spleen is found slightly enlarged from the first, and shows no further increase as the disease progresses; epistaxis and deafness are absent. The puerperal septicæmia often ends fatally after a few days — from four to ten days — or if recovery take place, the fever symptoms subside at an earlier date than is the case in enteric fever. In doubtful cases bacteriological examination of the blood will not help us much, as there may be a mixed infection of enteric fever and septicæmia. Some of the most difficult cases are those in which during or after some pelvic inflammation or mild septic poisoning enteric fever gradually supervenes as an independent event.

Acute gastro-intestinal catarrh may, if the fever be high, and remain so for a few days, as not infrequently happens in the young and in children, give rise to symptoms like a mild or abortive attack of enteric fever. The difficulties of diagnosis become especially great at the time of an epidemic of enteric fever, when many mild and abortive cases are about.

The *malarial* affections which occur in this country can scarcely be mistaken for enteric fever; in the remittent type of the severe malarial affections as they occur in tropical climates the presence of the plasmodium in the blood would form a pathognomonic sign.

Other affections with which enteric fever may occasionally be confounded are — acute rheumatic arthritis (especially during the first week, when severe pains in the joints may be present), *mania*, *perityphlitis*, *hæmorrhagic colitis*, *pelvic cellulitis*, *epidemic cerebro-spinal meningitis*, *extravasation of urine*, *acute trichiniasis*.

In discussing diagnosis, we may remark that sometimes patients present themselves for treatment with symptoms of sequelæ of enteric fever, in whom the enteric fever had not been diagnosed. The case of intestinal obstruction already quoted is an instance in point, and other cases, especially some with prominent nervous symptoms, could be cited.

Pathological Anatomy. — We have to distinguish between the lesions which are characteristic of enteric fever, those which are common to most acute febrile infections, and those which are the result of secondary infection or complication.

The characteristic changes are seen in the intestines, mesenteric glands, and spleen.

Intestines. — The lower part of the ileum is the portion affected, and here the parts close to the ileo-cæcal valve are more markedly affected than those higher up. In some cases the large bowel may show a few diseased patches, and occasionally the jejunum and even the duodenum may be the seat of the characteristic lesions. The affection is to a great extent confined to the follicular apparatus — the solitary follicles and Peyer's patches — and consists at first in a hyperæmia, followed by an infiltration of the glands with cell elements; the infiltrated patches then undergo necrosis, the typhoid slough forms, and becomes detached, and an ulcerated surface is left behind which undergoes cicatrisation. Considering these several stages more in detail, we have first, and for a few days only, marked hyperæmia of the affected part, the mucous surface appears swollen and red, and is covered by an abundant secretion of mucus. As cell infiltration takes place the hyperæmia disappears, the blood-vessels becoming compressed; the mucous surface is now paler, and the follicles and Peyer's patches stand out prominently. This is the *stage of infiltration*, which reaches its height from the 8th to the 12th day. Microscopic examination with the usual staining agents (eosin and hæmatoxylin) shows the follicle filled with cells of the type of leucocytes, many having one large, well-stained nucleus; in others the nucleus is badly stained and pale, and this infiltration extends slightly into the neighbourhood of the follicles; the walls of the blood-vessels show infiltration, and are compressed; the lymphatic vessels are dilated and filled with cells, and we see in them large ovoid cells with large nuclei — the proliferating endothelial cells. In a section stained with aniline dyes for the detection of micro-organisms, large numbers of typhoid bacilli are seen, most numerously in the centre of the follicle where the cell nuclei appear less stained; we notice them also collected in large numbers in the lymphatic vessels of the follicle, and can trace a few into the submucous tissue. When this stage has reached its height (10th–12th day) we may have in mild cases a gradual resolution; the cells which infiltrate the follicular apparatus undergo necrosis or fatty degeneration, and become absorbed. This process may be unaccompanied by ulceration, or by a few superficial erosions only with slight hæmorrhage. In most cases, however, as the swelling of the gland is considerable, the necrosis of the cells (which is a true coagulation necrosis) leads to the formation of smaller or larger *sloughs*, which are of yellowish or grayish colour, soft, and raised at the edges; these when microscopically examined are found to consist of granule cells, detritus, fibrin, red blood corpuscles and sundry micro-organisms. The slough gradually becomes detached and an *ulcer* is left (third week of fever). The ulcer is either round (solitary follicle or partial necrosis of Peyer's patch) or oval (Peyer's patch), with its long axis corresponding to the long axis of the intestines; the floor is usually smooth, and consists of the exposed muscular coat; sometimes the floor is irregular and shreddy, but it is not hardened or

much infiltrated; the edges are not indurated, they are often undermined, and float when the ulcer is held under water. The depth of the ulcer varies according to the extent of the necrosis. The serous surface of the intestine shows no changes.

Microscopic examination of a section of the affected part shows that the tissue of the intestinal wall adjoining the follicles and floor of the ulcer is filled with mononuclear cells and blood corpuscles; it presents all the appearance of embryonic tissue.

The number of ulcers varies considerably. I have twice seen a solitary ulcer, situated near the cæcum; in ordinary cases they are more numerous near the ilio-cæcal valve, and farther from this site they become smaller, and often more shallow.

In a few cases the lesions of enteric fever have been found, with the exception of intestinal ulcers; the Peyer's patches in these cases presented swelling and congestion only. Death in the cases reported had occurred at a date (after the 21st day) when the ulceration ought to have been well marked (69). We may assume that in these cases little phagocytic action is opposed to the typhoid bacilli in the walls of the intestines, and that they pass through to the mesenteric glands.

Cicatrisation of the ulcer occurs in the last stage; small granulations form, which gradually become changed into firm fibrous tissue. From the neighbouring part of the mucous surface an epithelial covering extends, and the glands may to some extent become regenerated. The cicatrix scarcely ever tends to narrowing of the lumen of the gut; it is smooth, depressed, and pigmented, and may be often recognised years after the occurrence of the enteric fever.

Mesenteric Glands. — Here we observe a process very similar to that seen in the follicles. At first the glands are slightly enlarged by hyperæmia, especially in their peripheric part; then they swell considerably, and become paler and softer (cell infiltration). The infiltrated cells then undergo fatty degeneration and become absorbed, and the gland gradually diminishes and becomes firmer. Occasionally the gland may undergo suppuration, which is probably due to a septic infection, though the typhoid bacillus may cause suppuration; the pus may burst into the peritoneal cavity, causing peritonitis, or it may become inspissated, and eventually form a calcareous mass. A man, who two years before had passed through a severe attack of enteric fever, came under my care for intestinal obstruction; the symptoms pointed to an obstruction of the small intestine, and an operation was performed: the cause of obstruction was then found to be a large mesenteric gland which had become adherent to a part of the small intestine, and had dragged in a portion of the wall of it, causing marked diminution of the lumen.

The *spleen* shows similar changes. It gradually increases in volume, and by the end of the third week may be three to four times its normal size and weight; the swelling is less marked in old people. During the first week there is hyperæmia. The capsule becomes stretched, and on section the spleen has a cherry-red colour, and the stroma is indistinct;

gradually the pulp becomes softer, bulges forward, and the Malpighian bodies appear distinct and larger (third week); with the fourth week, or sometimes later, diminution begins, the pulp appears pale or brownish, the consistence of the spleen becomes increased, and later still the stroma becomes more fibrous. Histologically we find at the height of the disease an infiltration of leucocytes, some of them degenerated, large endothelial cells with one or more nuclei, and large cells containing several red blood corpuscles. The typhoid bacilli are found disseminated through the spleen, and are often found in clumps.

The *tonsils* and the glands in the pharynx are found enlarged and infiltrated, but as this affection is seen in other acute infective fevers, it cannot be looked upon as a lesion specific to enteric fever.

The *medulla of bone* resembles in its structure the pulp of the spleen, and as in certain maladies (Hodgkin's disease, leucocythæmia) the glands, spleen, and medulla of bone are often alike implicated, some observers have laid stress in enteric fever on changes in the medulla of bone comparable with those of the spleen. These changes, however, have been found in other affections accompanied by profound disorders of the blood, and have nothing specific in character. Yet a close connection between the typhoid bacillus and bone is suggested by the frequent occurrence of osteitis, osteoperiostitis, or abscess of bone, which so often follow in the wake of the disease, and in them the typhoid bacillus has been found (see section on Symptomatology).

I will now briefly touch upon the lesions found in the other organs in enteric fever, omitting those affections, the nature and appearance of which is sufficiently evident during life, and a description of which will be found under Symptomatology.

Digestive Tract. — The stomach is often the seat of catarrh. Cornil (18) describes cell infiltration of the adenoid tissue, and compares it to the intestinal lesion. Handford (37) noticed similar changes and hæmorrhages. The *cæcum* and *colon* may occasionally show enlargement of the solitary glands and there may be ulceration also of the appendix; the rest of the large intestine is often the seat of catarrh, and occasionally ulcers are noticed, which may go on to perforation, which is less serious than perforation of small intestines; perforation of the rectum has been found with formation of recto-vaginal fistula. I have once seen marked hæmorrhagic infiltration of the greater part of the large intestines. The *liver* is not found enlarged, it is pale in colour and the gall-bladder is moderately filled with light coloured bile. Histologically we find more or less marked granular degeneration of the liver cells, and small necrotic areas; the capillaries are sometimes found dilated, and when death has taken place at a late period of the fever we find slight perilobular cell infiltration in the portal canals. Chantemesse describes small foci of cell infiltration in the central part of the lobule with degeneration of the adjacent liver cells. Typhoid bacilli are often seen in large numbers filling up the capillaries (56).

Acute yellow atrophy of the liver and abscess of the liver may be cited as very rare complications. The gall-bladder and large bile-ducts

may be the seat of catarrh. We may have, as rare complications, suppuration, ulceration, and perforation of the gall-bladder; more commonly the catarrh of the gall-bladder leads to the formation of gall-stone.

The spleen may be the seat of infarcts which may form pyæmic abscesses; in persons who have died after many weeks from exhaustion owing to long-continued suppuration (bed-sores, empyema), lardaceous degeneration of the spleen and other organs may be found.

Lungs. — Besides the affections mentioned under symptoms, we notice at times hæmorrhagic infarcts in the lungs and occasionally gangrene or pyæmic abscesses.

Heart. — The heart is flabby, pale in colour, and soft in consistency, sometimes almost friable. Microscopic examination reveals a variety of changes; in some cases no noteworthy alteration in the myocardium is found, in others there are changes in the muscular fibres, interstitial tissue, and blood-vessels. The muscular fibres may show fatty degeneration and occasional waxy degeneration; in some cases of sudden death segmentation of the muscular elements (*myocardite-segmentaire* of Renaut) has been noted; in cases in which the fever has run a more protracted course, small pigment granules in the neighbourhood of the muscle nuclei have been observed; hyaline (Zenker's) degeneration is rare; intermuscular cell infiltration is occasionally seen, and the small arteries of the myocardium may be the seat of endarteritis (77). Chantemesse and Widal have found typhoid bacilli in the heart-muscle. The *endocardium* and *pericardium* are not often found affected, though occasionally there may be both the vegetative and ulcerative form of endocarditis.

The Kidneys. — The changes in the kidney are manifold, and are not always in proportion to the renal symptoms exhibited during the disease. In some cases in which during life there was persistent albuminuria with casts, no noteworthy changes have been found; but in most cases, even with but slight albuminuria, we observe cloudy swelling of the epithelium of the convoluted tubes; in cases in which during life there have been signs of hæmorrhagic nephritis, or in which from the first there have been grave renal symptoms, the changes are marked. The kidneys are enlarged, especially the cortical part; the epithelium of the convoluted tubes is granular. Renaut describes a distension of the glomerular cavities and adjacent renal tubes with an albuminous material. Perivascular cell infiltration may also be noticed. In cases with septic complications there are sometimes small cell accumulations round the blood-vessels in various parts of the kidney. These have been specially noticed by Wagner, and have been compared to multiple lymphomata: they represent, however, only microscopic abscesses, and may eventually lead to small visible abscesses. They are found more often in scarlet fever and diphtheria than in enteric fever. The typhoid bacillus and bacill. coli commun. have both been found in sections of the kidney.

Muscles. — The changes observed here have been noticed in other febrile affections, though perhaps more frequently found in enteric fever. Some of the muscles (recti abdominis, adductors of the thigh, pectorales,

diaphragm) appear pale and waxy to the naked eye, and microscopically examined show Zenker's hyaline degeneration. A muscle so affected may rupture and give rise to hæmorrhagic extravasation. Other muscles show fatty degeneration, especially when fever has continued for weeks. Another change consists in a proliferation of the muscle nuclei. According to Metschnikoff, this appearance is due to an infiltration with leucocytes (phagocytes) rather than to a nuclear proliferation.

Nervous System. — Most of the nervous symptoms during the fever are due to the toxic products of the typhoid bacillus, which give rise to no anatomical changes; yet certain alterations have been found, such as œdema of the membranes and of the brain itself and distension of the ventricles, pigmentations of the ganglion cells, infiltration of the perivascular spaces with leucocytes, and of the spaces round ganglion cells, fatty degenerated nerve fibres and hæmorrhages (meningeal and cortical). Meningitis rarely complicates enteric fever. The pathological anatomy of the nervous affections occurring during convalescence (peripheral neuritis, sclerosis, etc.) need not be described here.

Pathological Physiology. — Much on this subject is still very obscure. The bacilli, after they have reached the intestines, multiply, penetrate into the mucous and submucous coats, invade the lymphatic tissue, and pass thence through the lymph channels into the mesenteric glands. Some of the bacilli reach the blood and pass to internal organs, principally the spleen. The bacilli produce various poisons, at present hardly known; some of these have a pyrogenetic action, and thus produce the fever. As a result of their irritant action and that of their products we get the intensely inflammatory signs in the intestines leading to necrosis.

The fever during the first eight to ten days is most likely due to the direct action of the bacilli and of their toxins. During the second and third weeks, when the intestines are ulcerated, another factor concerned is probably the absorption of some septic material into the blood, co-operating with the specific poison; the various complications which so often accompany enteric fever probably also add their quota. The diarrhœa is partly due to the irritation produced by the ulcers, but chiefly to catarrh of the large intestine with increased peristalsis. As it has been distinctly proved that typhoid bacilli may by themselves give rise to suppuration, we have an explanation of the occurrence of abscesses during or more especially after the attack. Lastly, as has already been pointed out, both when considering the etiology and the symptomatology of enteric fever, some of the symptoms, and especially many of the complications, are to be traced to other micro-organisms, which find a favourable soil for growth and development in the tissues and organs of the patient whose resistance has been much reduced by the fever.

As yet the numerous experimental investigations with injections of typhoid bacilli, of bacterium coli, of serum from immunised animals, etc., have not helped us much in clearing up the pathology of the disease, nor has the chemical examination of affected organs led to a clearer

understanding. Fenwick (25) extracted from the spleen of typhoid cases three varieties of chemical substances: albuminoses, alkaloids and fatty bodies; the injection of the albuminoses into lower animals caused a rise of temperature for thirty hours, with anorexia and emaciation, but no further changes of importance were noticed, whilst the injection of the alkaloids and fatty extracts was unattended by any results.

Prognosis. — Enteric fever, even in its mildest form, must be looked upon and treated as a serious disease; for even in mild cases death may occur from perforation, or from hæmorrhage, and sudden death without any premonitory symptoms, and for which no adequate cause can be found on autopsy, is occasionally seen. Perforation may occur during convalescence. As a relapse may occasionally be fatal, and as serious complications may occur during convalescence, the patient cannot be considered out of danger till convalescence is complete. We have further to bear in mind that however mild the fever may appear during the first and second weeks, grave symptoms are none the less likely to appear before the third week; no case therefore, however slight the symptoms at first, should be lightly treated. Some general propositions, however, may be stated as regards prognosis. As regards *age*, we may say that the older the subject the more unfavourable the prognosis: as regards sex authors differ somewhat; according to many the affection is more serious in women than in men. The prognosis is less favourable in stout than in lean people, and very unfavourable in drunkards, in persons who have undergone great privation and fatigue (soldiers in war), in persons with weak or dilated hearts or who are affected with valvular affections of the heart, or who have incipient phthisis or diabetes; the prognosis is also grave in pregnant and puerperal women. In persons of marked neurotic disposition, acquired or inherited, the nervous symptoms and sequelæ are to be feared; and in those affected with renal disease aggravation of this disease and uræmic symptoms are apt to occur. Septic complications are to be feared in those who suffer from surgical diseases, especially suppurating wounds; and in those who live in unhealthy or insanitary districts. It is also a well-known fact that in hot weather the disease is often more serious than in cold weather. During the decline of epidemics of enteric fever, as in other infectious diseases, the cases become less and less serious. Certain families show a particular disposition to enteric fever, several members of the same family may be attacked at the same time, and other members readily contract the disease (see Pfeiffer, Wagner). Recently with Dr. Wm. Sellers, junior, of Radcliffe, I saw two cases in the same family: in this family no less than five members had been attacked by it at various times; one contracted it by assisting in the laying out of the body of a relation who had died of enteric, and another had had it twice.

Apart from these general considerations, we are guided in our prognosis —

1. By the pulse: a slow, regular pulse indicates a favourable course;

an irregular and intermittent pulse, even if not high, is a grave omen, as it may denote myocarditis; a very quick and small pulse, except in young children, is an equally unfavourable sign, and if the pulse reach 140 or more in an adult, the issue is almost always unfavourable; a short and weak first sound, at the apex of the heart, or disappearance of the first sound, is a grave symptom; a soft systolic bruit, limited in extent and not due to previous endocarditis, is of no special significance.

2. By the temperature: in young, strong subjects a high temperature, say 104·5°–105°, if it only last for a few hours and rapidly fall to a lower temperature, and if the pulse be not very quick, is of no serious importance: if, however, the temperature remain high for some time, and especially if the fever be accompanied by nervous symptoms, and not quickly reduced by antipyretics, it is to be looked upon as very serious. Hyperpyrexia is a very unfavourable symptom, especially if after the application of cold the temperature does not fall much and rises very quickly afterwards; sudden fall of temperature, with the pulse remaining high, often denotes hæmorrhage or collapse.

3. By the nervous symptoms: low, muttering delirium, subsultus tendinum, convulsions (in adults), and incontinence of fæces and urine are of very grave omen.

4. By the intestinal symptoms: diarrhœa only becomes serious when it persists and is very profuse. Of the gravity of hæmorrhage and perforation we have already spoken.

Such complications as extensive pneumonia, pulmonary œdema, œdema of the glottis, hæmorrhagic nephritis, and symptoms of septic infection, are of serious import.

Special attention has been drawn to *sudden death* in enteric fever; it occurs in about 4 per cent of the fatal cases, and generally about the end of the third week. Excluding sudden or rapid death from perforation, in about two-thirds of the cases changes have been found post-mortem, such as embolism or thrombosis of the pulmonary artery, myocarditis, and degenerative changes in the myocardium, sufficient to account for the sudden death; in about one-third no such changes could be found. Some think that death is due to syncope caused by reflex influence from intestinal lesions, others (Laveran) attribute the death to cerebral anæmia. The premonitory symptoms are sudden dyspnœa, irregularity of the pulse, and syncopal attacks (20).

Mortality from Enteric Fever.—Numerous statistics exist on this subject (see Table II., Appendix). I will allude here only to a few of the more important points. The mortality per population has markedly decreased in England, but the mortality of the number of persons attacked with typhoid, or (to apply a term used by continental observers) the mortality compared to the morbidity, is still for England as high as it was in Murchison's time, namely, about 17 per cent. From 1848–1870 it was 17·26 per cent, according to the return of the Registrar-General, and also according to the report of some of the larger fever hospitals (see table for Monsall Hospital return, Appendix). In

the Cork Fever Hospital the mortality (1871–1890) was 8·6 per cent; the mortality in the Glasgow Fever Hospital was 17·29 per cent. The statistics of some of the larger continental hospitals when compared with those of English hospitals, show in many, like those of Berlin and Paris, a mortality slightly less; thus in Paris for 1882–88 it was 14·1 per cent, though since then it has risen to 20·6 per cent; in Berlin it was 14·5 per cent; in Leipzig (for 1880–1893), 12·7 per cent, whilst other places (such as Hamburg) show a much smaller mortality. To establish anything like a mean mortality in enteric fever is most difficult; it varies from year to year, and it varies with the age and sex of the patient. Contrary to Murchison's views, most observers (Griesinger, Gesenius) are agreed that amongst very young children the mortality is high; in persons from ten to thirty years of age it is much less, but it increases again in persons over thirty. The mortality is higher in women than in men; thus, according to Hayem, the mortality in Paris for 1888–1893 was of men (over fifteen years of age) 19 per cent; of women (over fifteen years) 22·5 per cent. In pregnant women (91) the mortality was 17 per cent, abortion occurring in 66 per cent; on the introduction of the cold bath treatment it fell to 6 per cent, with 55 per cent abortions; in puerperal women the mortality is nearly 50 per cent. The mortality amongst soldiers, as given in the reports of the various military hospitals, is better fitted for statistical purposes, inasmuch as the reports deal with persons in the prime of life and living under the same conditions. The mean mortality (from 1875–1891) in the French army, as given by Brouardel, was 12·2 per cent, and during these seventeen years it only varied between 11 per cent and 14 per cent.

It is of great importance to know how far the various methods of treatment affect the mortality. To arrive at a satisfactory conclusion we must not consider results obtained from a limited number of cases in one locality or observations made during one epidemic. The evidence appears now to be conclusive that the hydropathic treatment carried out strictly after Brand's method has considerably lessened the mortality. Thus in the Prussian army the mortality fell from 25 per cent to 8 per cent, and in the various hospitals, both in Germany, France, and America, where this system was rigidly carried out, equally satisfactory results were obtained (93). Thus —

	Per cent
Drasche (Vienna) found a reduction from .	16·2 to 9·3
Tripier and Bouveret (Lyon) found a reduction from	25 to 7·5
Osler (Baltimore) ,, ,, ,,	21·8 to 7·4
Thompson (New York) ,, ,, ,,	19 to 7·

And lastly, Vogl (Munich garrison) gives the following statistics: —

	Per cent
For 1841–1860	21
,, 1860–1875, treatment, partly expectant, partly by cold bath .	15·2
,, 1875–1881–2, treatment by bath and combined . . .	6·5

It must, however, be noted that the cold bath treatment in some of the larger German hospitals has not reduced the mortality to so low a level as in the list given above.

The antiseptic treatment, so much recommended of late by some clinicians in England, has not as yet produced any marked diminution in the mortality of typhoid; but I do not know how far it is adopted in the larger fever hospitals. At the Monsall Fever Hospital at Manchester, where the mean mortality is about 17 per cent, the mortality fell during one year, when this treatment was extensively used, to 13 per cent; and some physicians, like Dr. Caton of Liverpool, dealing with a smaller number of cases, have recorded even a much lower mortality.

Treatment. — We have as yet no specific treatment of enteric fever. We do not know of any drug which destroys the typhoid bacillus, or checks its growth in the intestinal glands and other organs; nor of any agent to counteract or neutralise the action of the toxins of the bacillus circulating in the blood. (The treatment recommended by Simmonds is mentioned further on.) In our treatment we must therefore try to put the organism into a state in which it can successfully withstand the action of the poisonous products, and maintain it there; we must also try to prevent, if possible, the ingress of septic organisms into the system, and of toxic bodies which result from abnormal fermentation processes in the intestines.

In speaking of the treatment of enteric fever it is well to consider, first, the management of the patient as regards hygienic conditions, diet, etc., and then to review special treatment by drugs, baths, etc.

Hygienic Measures and Management of the Patient. — The patient should be put to bed as soon as the symptoms show themselves. The bedroom should be large, airy, and well ventilated; it should be in a quiet part of the house; it should not contain too much furniture, and should have no carpets or bed-hangings. It is well to have two beds in the room, so that the patient may be changed from one to the other; especially is this useful when the patient is treated with the cold pack. The patient should rest on a spring mattress, and a mackintosh be placed beneath the sheet; he should only be lightly covered, and the temperature of the room be kept between 60° and 65°. In hot weather the temperature of the room may be artificially reduced. The patient should not be allowed to get up, and should be made to use bed-pans; he should be as little disturbed as possible, and not examined oftener than necessary, the right iliac region in particular should be rarely and gently handled; to prevent hypostatic congestion his position should be changed. The trunk and limbs should be sponged with vinegar and water (at 85°–90° F.) night and morning; the mucous membrane of the mouth kept clean, and gargled with boracic acid, or with the following mouth-wash (Acid boracic ʒj., Potass. chlorate ʒj., Glycerini ʒj., Aquam ad ʒvj.), or the parts painted with boroglyceride; for the teeth the same wash may be used. Special care should be taken to prevent the formation of bed-sores by washing the nates and adjacent parts with weak spirit or

spirit of camphor. As soon as erythema appears water or air cushions should be used, and the parts dusted over with boracic acid or salicylic acid and prepared chalk. The patient should not be left alone, and if there be any active and violent delirium he should be treated with consideration and yet with firmness; he should never be strapped or otherwise fastened down, put into jackets, or otherwise restrained. Under urgent circumstances, and for a short time, the sheet may be tightly drawn over him and fastened on both sides; but the proper means is to add to the number of the trained nurses. The window should be stopped so as to open no more than six inches, or a heavy table may be put in front of it.

Diet. — The diet should be nourishing, yet easily assimilable and non-irritating, and the food given often; the secretions of saliva, gastric juice, pancreatic juice, and bile being diminished, and the intestines ulcerated, we have to be very careful in the selection of the diet. Milk is an excellent food in enteric fever; it is as a rule well borne, and should be given throughout the whole course of the illness. Two to three pints in the twenty-four hours is a sufficient quantity; patients will often take more, but then the milk may be seen partly digested in the stool. The stools should be inspected, and the quantity of milk reduced if many curds are found. It is well to give it diluted with lime water or soda water, or other aerated water, and administered about every two hours. Or it may be given in weak tea, or in the form of custard, or whey or junket beaten up with egg. Some people cannot take milk, then peptonised milk, Benger's food, or arrowroot may be given instead.

Besides milk the patient may take broth, such as chicken or mutton broth, beef-tea, chicken jelly, and some of the other jellies, artificially prepared extracts, or cold meat or chicken juice, made by macerating finely chopped lean meat or chicken in water; some hydrochloric acid and a little salt being added, and the whole strained through a cloth. If there be much diarrhœa beef-tea or even mutton broth had better be avoided. Fruit is inadvisable especially if there be diarrhœa; but occasionally grapes, with skins and seeds removed, are much enjoyed and help to clean the tongue. As a *beverage* give pure water (which has been especially recommended in very large quantities by recent writers) or barley water, or toast and water, or water containing the white of raw egg strained through a cloth; weak tea to which milk is added, or iced coffee may be given, especially when the stomach is irritable, and the pulse flagging; aerated waters also may be allowed, except in those cases in which there are much flatulency and tympanites.

Alcoholic stimulants need not be given unless there are special indications for it: such as failure of the heart, pulmonary œdema or congestion, insomnia, low muttering delirium, threatening collapse, or very high temperature. In tipplers stimulants are often necessary from the first, and should be given to avert some of the graver symptoms which so often threaten them. When the cold bath is given or the ice pack, alcohol may be required before and after especially if the patient be

very weak or feel exhausted or faint. Alcohol is also needed when certain complications arise, such as perforation or hæmorrhage, which lead to collapse. The best form of stimulant is brandy or whisky; the quantity depends on the age of the patient and the gravity of the symptoms; three to four ounces in twenty-four hours usually suffice for adults. When the pulse becomes small and thready much larger doses, even ten to twelve ounces or more, may be necessary. Alcohol should be given soon after some food is taken; or it may be taken in the milk every two or three hours; in critical cases every hour. Its effects should be watched and the large doses diminished as soon as the desired effect is produced; of this the pulse is the best index, which should become stronger and slower. In some cases in which brandy is disliked we may give champagne or good claret. Alcohol should be withheld if signs of hæmorrhage from bowel or kidney appear, or if the urinary secretion become very much diminished.

Medicinal Treatment. — In mild cases, when the temperature does not exceed 102·5°, no medicine may be needed; some physicians give small doses of hydrochloric acid and quinine, and if the patient come under treatment before the 9th day, several doses of calomel (gr. ij. to gr. v.) over two or three days. This administration of calomel, recommended by Wunderlich, Liebermeister and others, appears to prevent a further rise of the fever, and to diminish the diarrhœa during the subsequent period; I have tried it also with good effect in the Monsall Fever Hospital. In the severer cases many physicians still follow an expectant treatment, and only treat such grave symptoms as pyrexia, profuse diarrhœa, etc., as they arise; others follow a particular line of treatment, which in its conception is either *antipyretic* or *antiseptic*, or a combination of both.

Antipyretic Treatment. — We have various means of lowering febrile temperature, and I would distinguish particularly between the antipyretic treatment by means of the cold bath or allied methods, and that by means of antipyretic drugs.

A certain amount of pyrexia is an essential element in fever and is looked upon by many persons as beneficial; it probably does interfere somewhat with the further growth, development, and action of the typhoid bacillus and its products, and it is said to increase the resistance of the organism. On the other hand, we know that a high temperature in itself is directly injurious to many organs, and occasionally the cause of severe nervous disturbances, though many of the grave nervous symptoms may occur with moderate temperature. Most observers are agreed that a high febrile temperature requires active interference. Now the method of reducing the temperature is by no means a matter of indifference. Abstraction of heat without much diminishing the production of heat, which to a large extent is caused by the oxidation of the tissues and by increased tissue metabolism, is the safest and best way of reducing the temperature; and the application of cold, especially in the form of the cold bath, best fulfils the requirements. There can be

little doubt that whenever this treatment can be applied it is far preferable to antipyretic treatment by drugs; and a comparison of the mortality statistics of the cases in which the cold bath treatment is carried out, with those of cases in which antipyretic drugs are administered, clearly shows the superiority of the former method of antipyretic treatment (12 to 16 per cent compared to 6 to 10 per cent). Some of the best English clinicians, like Sir Wm. Jenner and others, are not in favour of the cold bath treatment. Yet a glance at the tables published by the Registrar-General, and by the several Hospital Boards in England, must satisfy every one that, whilst the mortality is much diminished, the mortality from enteric fever per case rate in England, in spite of better hygienic conditions and management, is still very considerable.

The *cold bath* treatment, first recommended by Currie in 1787, is now extensively used, especially on the Continent. Its reintroduction is due to Dr. Brand of Stettin (1861), who showed how the mortality of enteric fever was lessened by its adoption; and his method was soon followed in a more or less modified form by other observers. In England Dr. Cayley has most strongly advocated the use of the cold bath in enteric fever (12). Brand recommends it to be used whenever the temperature is over 102° (measured in the rectum), and this treatment he adopts from the very beginning.

Before the patient is put into the bath the face and chest may be sponged with cold water, and if the patient be weak and exhausted he receives some stimulant. The temperature of the bath varies from 70° to 65° F., the bath is placed close to the bed, and the patient is lifted into it and so immersed that the water covers the chest; the back of the patient is supported by a water cushion, and a sheet or napkin is folded round the loins. The head and forehead are now covered by a cloth wrung out in cold water, and whilst the patient is in the bath cold water (of lower temperature than that of the bath) is applied to the head every three to four minutes, whilst the limbs and thorax are rubbed during the whole time of the immersion. While in the bath the patient has some cold water to drink. The duration of the bath is from ten to fifteen minutes as a rule; the patient is then lifted out and dried gently, except over the abdomen, put into bed lightly covered, and hot bottles are placed at the feet. A second dose of some stimulant, such as whisky and hot water, is then given to him. During the bath the state of the patient must be carefully watched; with the fall of the body temperature he begins to shiver; but if the temperature before the bath has been very high, he may still be left for some minutes longer whilst the limbs and thorax are more vigorously rubbed. If the pulse be very weak, and the patient become cyanotic, he should be removed from the bath at once. After the bath the patient may take some food, and he generally then falls into a quiet slumber; if not, Brand recommends the application of compresses wrung out in cold water to the chest and abdomen. Half an hour after the removal from the bath the temperature is taken; it is usually found to have fallen 1° to 3° F.,

and if in two or three hours the temperature again exceeds 102·2° the bath is renewed. Brand has given as many as eight baths in the twenty-four hours, but usually four to six suffice. The good effects of the cold bath are readily seen: the pulse becomes slower and the tension of the artery is increased, the number of respirations diminish, the tongue becomes moist, and the appetite improves; the nervous system is especially relieved, the delirium disappears for a time, the patient appears much calmer, and the sleep becomes more natural. The advantages claimed for the cold water treatment are: that the fever runs a less protracted course, that grave nervous symptoms are less apt to occur, that the heart and pulse remain strong, that the tongue remains moist and the appetite good, and that the diarrhœa, if not lessened, is certainly not increased: statistics show that the mortality is less. The cold bath is contra-indicated when the pulse is irregular and intermittent, and when we suspect myocarditis or pericarditis; also in intestinal hæmorrhage occurring during the later stage, in peritonitis, and in old people. On the other hand the puerperal state, pregnancy, bronchopneumonia, pneumonia, intestinal hæmorrhages during the first week, and albuminuria, are no contra-indications (Chantemesse). Relapses appear, however, to occur more frequently with the cold bath treatment.

Brand's system of treatment is still carried out by a good many medical men, especially on the Continent. Many physicians, however, do not bathe the patient unless the temperature reach 103° or 103·5°: many also advise the use of water of 80° F., the temperature of which is gradually lowered to 70° or 65°; this plan appears to have many advantages, but it does not give quite as good results as the stricter method of Brand.

For the five years ending 15th May 1895, systematic hydrotherapy — the method of Brand with certain minor modifications — has been used in the Johns Hopkins Hospital at Baltimore. Each patient receives a tub-bath of twenty minutes at 70° every third hour, if the rectal temperature be at or above 102° 5′. Prof. Osler (67*a*) says: "Two advantages are claimed for hydrotherapy in typhoid fever — a mitigation of the general symptoms of the disease and a reduction in the mortality. Our experience during the past five years bears out these claims." Osler adds that the beneficial action is "not so much special and antipyretic as general tonic and roborant. The typhoid picture is not so frequently seen." About 6 to 8 per cent more lives are saved. While continuing its use the author says that he prays for a method which, "while equally life saving, may be, to put it mildly, less disagreeable."

In certain cases it is well to place the patient in a warm bath and to lower the temperature gradually by the addition of pieces of ice; these are cases of threatening syncope, or cases in which the breathing is very much oppressed from emphysema or laryngeal complications, or in which there is profuse sweating.

As the cold bath treatment is difficult to carry out in private practice, other modifications of applying cold to the body have been recommended; such as the wet pack, the ice pack, sponging the body with iced water, or

with cold water and vinegar, placing a cradle over the patient in which buckets containing pieces of ice are suspended (Fenwick), or Leiter's tubes, with iced water running through them, which are placed over various regions of the body, head, chest or abdomen. None of these procedures, except perhaps the ice pack, reduce the temperature so effectively as the cold bath.

Many physicians combine the cold water treatment with medicinal treatment. Jurgensen recommends the cold bath when the temperature reaches 104°, and gives quinine. Liebermeister gives calomel when the patient is seen early; he recommends a bath of 70° F. when the temperature in the axilla is over 102·2° F., and moreover large doses of quinine (20 to 40 grains in the evening). Bouchard combines antiseptic treatment with the baths, but the initial temperature of the bath is only about 5° F. lower than the temperature of the patient and is gradually reduced to 85°.

Partly as antipyretic, but more as hydropathic treatment, must be mentioned the *prolonged immersion in a tank bath*, recommended by Dr. James Barr of Liverpool (5).

The temperature of the bath, which varies from 90° F. to 98° F., is regulated according to the temperature of the fever patient, that is, the higher his temperature the lower the temperature of the bath; the patient is kept in the water for days (six to thirty-one days), and passes all his discharges into the bath. Dr. Barr claims all the good effects produced by the cold bath for his immersion treatment, which, on the other hand, avoids the objections usually urged against the cold bath: out of forty cases treated by him in this way only one died.

In England, and to some extent also on the Continent, the cold water treatment is principally confined to cases of hyperpyrexia, and for ordinary cases of enteric fever one or other of the antipyretic drugs is given when the temperature reaches 103° or 103·5°. Quinine is still much used; it should be given in one or two large doses daily, and only at those times of the day when there is a natural fall in the temperature, that is, evening and forenoon: the dose for an adult should be from 15–30 grains, for a child 3–5 grains. Antifebrin (4–8 grain doses) and phenacetin (10–15 grains) are now much preferred to antipyrin (10–20 grains), as the latter may cause the temperature to fall too rapidly, and induce symptoms of collapse and irregularity of the pulse. Salicylate of sodium (15–30 grains) was formerly given largely in enteric fever. At the Monsall Fever Hospital some years ago the late Dr. Tomkins, then resident medical officer, tried salicylate of sodium in a very large number of cases; but the depressing effects, the unpleasant accidents (such as delirium, vomiting, dyspnœa, etc.), and the tendency to hæmorrhage from the intestines which it produced, made us abandon its use. The antipyretics — antipyrin, antifebrin, and phenacetin — are given when the temperature is over 103° F., and repeated after some hours when the temperature has again risen. A combination of phenacetin with 2–5 grains of quinine is now very much used. Apart from the therapeutic

effect, it must be noted that a rapid fall of temperature after the administration of any of these antipyretics is as a rule a good prognostic sign. Quite recently two new antipyretics, malakin (44) and lactophenin (90) have been described, and the action of lactophenin in typhoid is much praised by v. Jaksch. Among other drugs which were formerly preferred, but which are now rarely applied as antipyretics, are digitalis and veratria. Kairin and thallin have marked antipyretic properties, and thallin is still occasionally used (78).

Antiseptic Treatment. — Of the various antiseptic remedies *calomel* was the first to be used, and is still largely used by some physicians. It was not given in the first instance on account of its antiseptic properties, but because under its use the duration of the fever seemed to be lessened, and its course to be milder. Of its antiseptic virtue there can be no doubt, and experimental investigations have shown that it readily kills bacteria, that it prevents butyric acid fermentation, — a fermentation brought about by micro-organisms, — that it checks the formation of products of decomposition usually found in the digestive tract (indol, skatol), and that it does not interfere with the action of the unorganised ferments of the saliva, gastric and pancreatic juices (Wassiljeff).

Perchloride of Mercury ($\frac{1}{2}$ to 1 drachm of the solution of perchloride of mercury, with 1 or 2 grains of quinine, given every four hours for several days) has been highly recommended by Sir W. Broadbent; especially when the motions are very offensive and accompanied by much gas, the abdomen much distended, and the fever high. Calomel or perchloride of mercury are only to be given for a few days; but within the last few years more thorough antiseptic treatment has been advised, and numerous drugs have been recommended, not so much with the object of checking the action of the typhoid bacilli which have already passed the intestines and reached internal organs, as with that of acting on any toxins as yet unabsorbed, and particularly of checking fermentation and the action of the numerous micro-organisms found in the alimentary canal, the growth and development of which are favoured by the presence of the typhoid bacillus, and the products of which may be absorbed through the ulcerated surface of the intestines.

One effect of the antiseptic treatment which is often apparent is that the dejections become less offensive, sometimes quite odourless; bacteriological examination of the fæces, however, shows that they still contain a very large amount of living micro-organisms. Diarrhœa is often diminished, the temperature reduced, and some of the graver nervous symptoms are said to be prevented. Whilst some speak very highly of the effects of the antiseptic treatment, and record a very low mortality, others have seen but little benefit from the treatment. My own experience from a number of cases in which the various antiseptics have been tried makes me think well of this treatment, though it is certainly inferior to the cold water treatment.

Of the various antiseptics which have been recommended we may mention —

β Naphthol, is given either alone in powders or capsules (5–10 grains every four hours), or mixed with salicylate of bismuth. 150 grains of β naphthol are mixed with 75 grains of salicylate of bismuth and divided into thirty powders. From three to twelve of these are given in the twenty-four hours. Teissier recommends besides, that four enemata with cold water be given daily to aid diuresis, and one enema containing 15 grains of quinine and an infusion of valerian (33). In cases in which constipation exists, *salicylate of magnesium* (50–100 grains daily) has been recommended.

Salicylate of quinine I have often given (10–15 grains) with good effect.

Salol (40–60 grains in twenty-four hours) has come much into use of late. It is usually well borne, produces in these doses no toxic effects, deodorises the stool, and often relieves flatulence and tympanites.

Betol, or salicylate of naphthol, *naphthalin*, and benzoate of β naphthol, or benzo-naphthol, have been highly spoken of by French observers. Hydronaphthol was recommended by Clarke; magnesium benzoate by Klebs; dermatol (17) by other observers.

Carbolic Acid.—2½–3 grains in keratin pills, or in the following mixture (14), Acid carbolic liquefact. (Calvert) ♏xij., Tr. iodi. (B. P.) ♏xvj., Tr. aurant. ʒiss., Syrup simpl. ʒiij., Aquæ ℥viij.; ℥j. may be given every four hours for the first fourteen days, or till the urgent symptoms yield, and then three times a day (Moore), or *creasote* may be used, in pills or capsules, 1 to 2 minims; or paracreasotic acid (51).

Turpentine acts both as an antiseptic and as a stimulant, it checks tympanites, and is especially to be recommended in hæmorrhage. It must be given cautiously if nephritis be present. A dose of 5–15 minims given in capsules, or emulsified with yolk of eggs, I have often found well borne, or a mixture of the same with spirit of nitrous ether and spirit of chloroform (Moore).

Chlorine is highly recommended by Burney Yeo. Into a twelve-ounce bottle put 30 grains of powdered potassium chlorate, and pour on it 40 minims of strong hydrochloric acid. Chlorine gas is at once liberated. Fit a cork into the mouth of the bottle, and keep it closed till it has become filled with the greenish yellow gas. Then pour water into the bottle, little by little, closing the bottle, and well shaking at each addition, until the bottle is filled. To 12 oz. of this solution 24–36 grains of quinine are added, and 1 oz. of syrup of orange-peel. Dose, 1 oz. every two, three, or four hours, according to the severity of the case.

Camphor is recommended by Janeway; *Thymol* has been also used (89).

Chloroform may be given internally, 1 part of chloroform in 150 of water (84, 98). Chloroform rapidly destroys typhoid bacilli.

Quinine must also be grouped with the antiseptic remedies.

Besides the antiseptic treatment of enteric fever we have yet to mention the administration of potassium iodide, which was very much in vogue on the Continent, as a remedy throughout the fever period, and is spoken of very highly; also the administration of large quantities of water

by the mouth (74), or in the form of enemata: Cantario recommended large enemata of cold water and gallic acid (5 to 100 of water).

The antitoxin treatment, successfully applied in diphtheria and tetanus, finds as yet no place in the treatment of enteric fever. E. Fränkel (28) in more than fifty patients suffering from enteric fever used subcutaneous injections of sterilised, attenuated cultures of typhoid bacilli, grown on beef-tea made from thymus gland; the injections which produced a distinct reaction were repeated several times. Fränkel states that the treatment shortened the duration of the fever, and altered the continued into a remittant form. This treatment can scarcely be looked upon as a specific treatment, for Rumpf obtained results similar to Fränkel's by using the products of other bacteria, such as the bac pyocyaneus. Local hæmorrhagic infiltration round the typhoid ulcers, the probable result of this treatment, has been noted by Kraus and Baswell.

Treatment of Special Symptoms and Complications. — I can only refer here to a few of the more important.

Hyperpyrexia. — All authors are agreed that there is but one plan of treatment for this event, namely, the cold bath. Where this is inapplicable, the ice-pack or cloths wrung out in iced water are to be applied to the limbs and trunk of the body, the cloths to be repeatedly changed till the temperature of the body is sufficiently reduced. At the same time large doses of quinine, 30–40 grains, may be given. This plan I found successful in two cases in which the temperature had reached 106·5° and 107° respectively.

For the *adynamic* form of fever subcutaneous injections of ether, caffein (subcutaneously or by the mouth, 1–3 grains), musk, or camphor may be used.

In the *petechial form* large doses of quinine, perchloride of iron, lime juice are prescribed.

Constipation. — Constipation lasting only a few days, and not accompanied by much tympanites and flatulency, need not be treated medicinally; an admixture of beef-tea and milk diet may be tried. If the constipation be more obstinate glycerine enemata or cold water enemata may be given; should these produce little effect, and the constipation have gone on for five days or more, small doses of castor oil (one to two teaspoonfuls in milk) may be given, and repeated after some hours if necessary.

Profuse Diarrhœa. — This may have to be treated if the alvine discharges amount to more than eight in the twenty-four hours, and if the patient is thereby rendered weak and exhausted. A starch enema, to which 20–30 drops of laudanum are added, often suffices to keep the diarrhœa within bounds; it causes diminished peristalsis in the large intestines, and often the diarrhœa is due more to a catarrh of the large bowel than to the ulcerated state of the small intestines. Nitrate of bismuth, salicylate of bismuth, and mistura cretæ are equally efficacious; but if they fail one need not hesitate to give opium, either alone or in

combination with acid (sulphuric acid preferred), or with acetate of lead or sulphate of copper. There is no objection to giving the opium with the lead or copper salt in the form of a pill; but it is better, perhaps, to give it in fluid form, so as to avoid mechanical irritation of the ulcerated surface in case the pill should not dissolve before it reach the affected part. As I have said, antiseptics, such as β naphthol, often subdue the diarrhœa quickly.

Persistent Vomiting. — Food should be given in small quantities and often. Milk and lime water or Benger's food may be tried, or some of the prepared foods, or cold meat juice with acid. Bismuth in powder (10 grains) with cocaine hydrochlor. (gr. $\frac{1}{4}$), given three to four times daily, I have often found very efficacious. A sinapism to the epigastrium may also be applied. Ingluvin in 5 grain doses has been recommended.

Pain in the abdomen may be relieved either by cold or hot applications to the abdomen. The latter, either as fomentations or poultices, are highly spoken of by some English observers.

Tympanites. — Often a troublesome symptom. Enemata with turpentine or tincture of valerian often give decided relief. Turpentine may be given internally in capsules of 10 minims. If there be much flatulence, carbolic acid, or creasote or sulphocarbolate of soda (15 grains) may be tried. The application of ice to the surface of the abdomen is highly recommended by Cayley. If the tympanites do not yield to any of these drugs, the introduction of a long tube may give passage to much flatus; but this operation has to be repeated, as its effects are often very temporary.

Hæmorrhage from the Bowels. — We have already spoken of the gravity of intestinal hæmorrhage when it occurs after the first week, and when it is profuse. The patient must be kept quiet in the recumbent posture, and a small dose of morphia ($\frac{1}{4}$ grain) should be injected at once. Ice should be applied to the abdomen (the ice may be placed between flannel, or small pieces of ice may be placed in a kind of square dish made out of a piece of mackintosh). The patient should suck small pieces of ice, and all his food should be iced. Milk should be stopped, or given with carbonate of soda, or in the form of alum whey, that is, mixed with finely powdered alum and the curds separated from the serum (21*a*). *Ergot* was formerly in general favour, but has fewer advocates now; it is best given as a subcutaneous injection of ergotin — 1 to 3 grains. Of much more service are large doses of acetate of lead, given every two to three hours, or gallic acid and opium. Turpentine in 10 minim capsules (1 drachm given two to three times a day) has given me by far the best results. It is also contained in the mixture recommended by Murchison. (Acidi tannici gr. x., Tinct. opii ℥x., Spirit. terebinthini ℥xv., Mucilag. ʒij., Tinct. chloroform. co. ℥xv., Aquam menth. pip. ad ℥j.; this dose to be taken every two hours.) Ice-water injections have also been tried with success. Opium enemata are to be recommended.

The profound *anæmia* which accompanies or follows profuse hæmorrhage is best treated by subcutaneous injections of ether, and if the

pulse become very frequent and small a large quantity of normal salt solution is to be injected into the subcutaneous tissue. The salt solution is contained in a tin or glass vessel held or suspended at some height from the patient, and connected by means of an indiarubber tube with a fine aspirating needle; this is inserted into the skin below the scapula, where the subcutaneous tissue is loose. As the salt water flows into the tissue under a high pressure, a large quantity, half a pint or more, can thus be easily injected. The operation can be repeated on the other side after a little time. A very marked improvement follows the injection, though too often it is but temporary.

In peritonitis, whether due to extension of inflammation or to perforation, large doses of opium are given and poultices applied locally; if accompanied with symptoms of collapse alcoholic stimulants should be given freely, ether injected, and heat applied to feet and legs.

As *perforation* is almost always fatal, and the medicinal treatment of little value, surgical interference (that is, laparotomy, washing out of the peritoneal cavity, suturing the intestines, or the establishment of an artificial anus) has been suggested. Van Hook (43) records one recovery out of four cases in which he operated. When he wrote nineteen laparotomies with four recoveries were recorded. It is very difficult to give the indications which render an operation likely to be successful. Those cases in which there is no great collapse, or in which the collapse and the more acute symptoms have passed off, but all the signs of peritonitis with exudation exist, appear the most favourable for operative interference.

Some of the various symptoms may require special treatment:

Persistent Insomnia. — Sulphonal, or trional in 15–25 grain doses rarely has much effect. Chloral and bromide act better, but should not be given if heart's action is weak; small doses of morphia may often be given with advantage, and without producing any ill effects; or paraldehyde.

In *Delirium.* — Ice to the head, a sinapism to the back of the head, and morphia with quinine; if of low muttering character, stimulants may be given.

Delirium tremens is best treated by large doses of paraldehyde, and occasionally morphia may be necessary.

Weakness of the heart's action, indicated by the pulse, and due to change in the myocardium or to general prostration, is best treated by digitalis, ether, citrate of caffein, and by subcutaneous injections of strychnia ($\frac{1}{30}$ of a grain). Digitalis may also be given with advantage in the form of digitalin subcutaneously, or in granules, but its effects on the pulse must be watched. Ziemmsen recommends subcutaneous injections of camphor dissolved in olive oil (camphor 1 gramme, olive oil 5 grammes).

In *acute dilatation of the heart*, if it occur in plethoric subjects, and especially if associated with pulmonary complications, cyanosis, and marked distension of the veins, venesection may be resorted to.

Bed-Sores. — These can be prevented by proper attention to the patient, as I have already said. The nurses should be able to lift the patient easily, he must not remain a moment wet or soiled, the buttocks must be washed (if danger threaten) once or twice a day with warm soap and water, and the skin disinfected with boracic acid and lanoline or other means. If the skin become rough, reddened, or show slight abrasions, the part may be washed with boracic acid solution or weak perchloride of mercury solution, and some ointment, such as zinc or boracic acid ointment, or iodoform powder, may be applied to the abraded part. If a slough have formed antiseptic and stimulating dressings, such as carbolic acid (1 in 40), or compound tincture of benzoin, or balsam of Peru are required. Over the lint, which ought to fit exactly into the ulcer, a piece of gutta-percha tissue is applied, and outside this again some folds of lint, and the whole fixed by a strip of diachylon plaster. When the slough is large it is best to dust it over with iodoform, or iodol, or aristol; this is covered by gutta-percha tissue, and over this lint dipped in an antiseptic or stimulating lotion is placed. The best preventive against bed-sores is to warn the head nurse that she will be superseded if they occur. [See article on "Nursing."]

It would be beyond the scope of this article to speak of the treatment of the many complications and sequelæ of enteric fever, such as pneumonia, pleurisy, nephritis, etc., as these subjects will be dealt with in the several articles on these affections.

Treatment during Convalescence. — Considering the nature of the lesion in enteric fever, and that the healing process can be but slow, the patient's progress during convalescence should be most carefully watched, and strict injunctions given as to rest, diet, and general management.

The temperature should still be taken for a fortnight, so as to judge of the progress of the case or foretell an impending relapse. The patient should keep to his bed for some days after the subsidence of the fever and till he feels sufficiently strong to get up; if there have been any heart symptoms he should keep to the recumbent posture even longer. Usually we may allow the patient to sit up for a short time about a week after convalescence has begun.

With the beginning of convalescence the stimulant should be at once reduced, and in young subjects may soon be stopped altogether. The diet for eight to ten days should still be chiefly of milk; soft boiled eggs may be allowed, and soups, milk puddings, and custards: if the diarrhœa continue during convalescence, even a longer period — about a fortnight — must elapse before the patient is allowed solid food; and then he should only be allowed to eat at first fish (whiting, sole), then such light food as chicken, pigeon, sweet-bread, tripe, before reaching beef and mutton. Stale bread or biscuits, and a small amount of vegetables (rice, mashed potato), and stewed fruit may be allowed with the solid food. Drugs are rarely necessary during convalescence. If diarrhœa persist, bismuth, opium and lead may be given; if on the other hand

constipation occur, cold water taken in the morning fasting, or a cold infusion of senna-pods, or stewed fruit, will often overcome it: if these be insufficient, mild laxatives (Hunyadi Janos, Carlsbad salts, etc.) should be administered. When the patient's recovery is very slow, and he suffers much from anæmia and weakness, the mineral acids, with quinine or nux vomica, may be given, followed by mild iron preparations. Change of air materially helps to complete the convalescence, but the patient should not leave his home for a month after the subsidence of the fever lest a relapse occur.

Prophylaxis of Enteric Fever. — Knowing the cause of enteric fever, the vehicles which convey it, and the factors which aid in its development, much can be done, and a good deal has been done (1) to *check outbreaks of enteric fever*, and (2) to *prevent the spread of the disease.*

With the first of these two propositions sanitary science has occupied itself for many years and with very good results; many of the epidemics have been traced to a contaminated water or milk supply. Defective drainage and impure water may play an important part in the production of enteric fever, but, as explained in the chapter on Etiology, they chiefly act by preparing, as it were, a favourable soil for the growth and development of the specific bacillus, and by rendering the body less resistant to its action. When enteric fever breaks out, it is advisable to boil drinking water and milk, and to skin fruit before eating it. As in many places on the Continent the sanitary arrangements as to drainage and water-supply are still far from satisfactory; and as travellers and new residents are more apt to be attacked with enteric fever in places where enteric fever is endemic, than the inhabitants of the district, who appear to acquire immunity from it, it is well that travellers to continental towns should abstain from drinking water and unboiled milk, and when eating raw fruit should remove the skin of the fruit.

To prevent the spread of the disease, when it occurs in an endemic form, from the patient to those who come in contact with him, is no difficult matter if proper care be taken; for it is well established that the fæcal discharges and perhaps the urine are the only excretions which contain the active agent. Sputum, if there be any, should also be disinfected. The following measures should be adopted: the dejections (both urine and fæces) are to be received into a bed-pan containing a strong disinfectant (1–20 carbolic acid), and a sufficiently large quantity of the disinfectant is to be added to the discharge and well mixed with it. The nates must be well cleaned with paper, or with linen moistened with dilute carbolic acid; this refuse is burnt or added to the contents of the bed-pan. The bed-linen, blanket, and body linen of the patient should be changed at once when soiled; they should be placed in a sheet soaked in carbolic acid (1 in 40), and afterwards kept for some hours in carbolic acid solution of the same strength: before they are sent to the laundry they should be well boiled. The feeding utensils are to be cleaned in dilute carbolic acid, and afterwards with boiling water. The nurse after attending to

the alvine discharges or changing the linen, and always before she takes her meals, should wash her hands in corrosive sublimate solution (1 to 1000). Every precaution should be taken after the death of a patient as regards the bed-clothing, sheets, etc. Mattresses, pillows and clothes should be sent to a disinfecting oven, when this is feasible.

Instead of carbolic acid as a disinfectant some use strong commercial hydrochloric acid or corrosive sublimate. Chloride of lime is an excellent disinfectant which quickly destroys typhoid bacilli, and it may be used to disinfect the fæces.

If there be any expectoration the sputa are to be dealt with in like manner.

JULIUS DRESCHFELD.

APPENDIX

TABLE I. — Annual Mortality per Million Persons living from Fever.

Period.	England.			London.		
	Typhus.	Enteric.	Ill-defined.	Typhus.	Enteric.	Ill-defined.
1838		1228			....	
1839		1010			....	
1840		1089			....	
1841		932			....	
1842		1004			620	
1843		....			1075	
1844		....			849	
1845		....			641	
1846		....			873	
1847		1807			1474	
1848		1266			1647	
1849		1044			1125	
1850		865			875	
1851		997			1000	
1852		1022			901	
1853		1008			1064	
1854		1015			1125	
1855		875			966	
1856		847			1045	
1857		988			838	
1858		918			716	
1859		806			675	
1860		652			531	
1861		767			656	
1862		919			284	
1863		874			988	
1864		960			1278	
1865		1089			1074	
1866		986			884	
1867		778			708	
1868		895			786	
1869	193	390	239	225	337	194
1870	147	388	233	147	303	177
1871	121	371	186	118	267	133
1872	80	377	145	52	242	97
1873	70	376	132	82	269	96
1874	74	374	130	91	256	98
1875	62	371	108	37	235	78
1876	48	309	81	45	217	57
1877	45	279	78	44	251	54
1878	36	306	71	41	283	54
1879	21	231	58	19	229	43
1880	21	261	58	20	186	35
1881	21	212	44	24	254	35
1882	36	229	39	14	252	24
1883	33	228	36	14	247	26
1884	12	236	28	8	284	20
1885	12	175	24	7	150	20
1886	9	184	22	3	154	18
1887	8	185	18	5	151	11
1888	6	172	15	2	169	9
1889	5	176	15	4	130	10
1890	5	179	13	2	146	9
1891	5	168	11	3	132	10
1892	3	137	8	3	102	5

TABLE II. — Death-rate from Enteric Fever per 1,000,000.

Year.	England.	London.	Manchester.[1]
1871	371	267	450
1872	377	242	400
1873	376	269	460
1874	374	256	390
1875	371	235	440
1876	309	217	420
1877	279	251	290
1878	306	283	310
1879	231	229	180
1880	261	186	260
1881	212	254	170
1882	229	252	250
1883	228	247	200
1884	236	234	190
1885	175	150	170
1886	184	154	290
1887	185	151	310
1888	172	169	330
1889	176	130	310
1890	179	146	270
1891	168	132	370
1892	137	102	240
1893	...	161	250

[1] The rates for the years previous to 1891 are for the Township of Manchester, and the Unions of Chorlton and Prestwich, which have been taken to approximately represent "Manchester."

TABLE III.—Enteric Fever: Monsall Fever Hospital, *26th August* 1884 *to* 25*th August* 1894.

	Males.			Females.			Males and Females.		
Age.	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Under 5 years.	39	2	5·13	31	5	16·13	70	7	10·00
5 years and under 10.	151 moribund 1 152	8 1 9	5·29 5·92	151	9	5·96	302 moribund 1 303	17 1 18	5·62 5·94
10 years and under 15.	200 moribund 4 204	15 4 19	7·50 9·31	183 moribund 1 184	17 1 18	9·29 9·78	383 moribund 5 388	32 5 37	8·35 9·53
15 years and under 20.	274 moribund 4 278	38 4 42	13·86 15·10	150 moribund 1 151	29 1 30	19·33 19·86	424 moribund 5 429	67 5 72	15·80 16·78
20 years and under 25.	224 moribund 5 229	41 5 46	18·30 20·08	128 moribund 1 129	19 1 20	14·84 15·50	352 moribund 6 358	60 6 66	17·04 18·43
25 years and under 30.	144 moribund 1 145	40 1 41	27·77 28·27	98 moribund 5 103	18 5 23	18·36 22·33	242 moribund 6 248	58 6 64	23·96 25·80
30 years and under 40.	118 moribund 6 124	34 6 40	28·81 32·25	77 moribund 2 79	18 2 20	23·37 25·31	195 moribund 8 203	52 8 60	26·66 29·55
40 years and under 50.	39 moribund 3 42	13 3 16	33·33 38·09	40 moribund 3 43	14 3 17	35·00 39·53	79 moribund 6 85	27 6 33	34·17 38·82
50 years and under 60.	3	1	33·33	11	3	27·27	14	4	28·57
Over 60.	1	..	..	2	..	..	3	..	..
All Ages.	1193 moribund 24 1217	192 24 216	16·07 17·74	871 moribund 13 884	132 13 145	15·15 16·40	2064 moribund 37 2101	324 37 361	15·69 17·18

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CHOLERA ASIATICA

Nomenclature.—The Hippocratic term cholera was originally employed to indicate bilious diarrhœa. It has come, in course of time, to be applied to any violent intestinal flux; such adjectives as simplex, biliosa, nostras, infantilis, serosa, spastica, perniciosa, epidemica, etc., being used to distinguish varieties. The qualifying adjective commonly added to the word cholera, in order to denote the disease which is the subject of this article, is founded on the circumstance that in some parts of Asia—or, more strictly, of India—it is perennially present; and that, when it makes its appearance in other countries and continents, it can always be traced back to its Asiatic birthplace and home. It is by this geographical title that serous, spasmodic, pernicious, epidemic cholera is known in all the languages of Europe. In India it is usually denominated by the vernacular term *haiza* (Hindostanee); other Eastern names are *Enerum Vandee* (Tamil), *Ookal Julab* (Deccan), *Vantee* (Telegoo), *Duba* (Arabic), *Ho-louan* (Chinese), *Visuchika* (Sanscrit).

Definition.—Cholera Asiatica may be defined as "a specific and communicable disease, probably due to a specific organism, prevailing endemically in some parts of India, and from time to time diffused epidemically throughout the world; it is characterised by violent vomit-

ing, purging, cramps, collapse, and suppression of urine, followed by febrile reaction; case mortality about 50 per cent."

History and Geography. — The authentic history of Asiatic cholera dates from the year 1817, when it broke out violently in Lower Bengal, and became the subject of close and exact observation. There is every reason to believe that previous to that date the disease prevailed in India, and spread at intervals throughout Asia as it does now; but it is very doubtful whether it overstepped Asiatic limits. Certain passages in Sanscrit, Chinese, Arabic, and Greek medical literature have been supposed to refer to it; but the descriptions of all writers before our own century are vague, and vary as the colliquative, spasmodic, febrile, or prostrating features of the malady chiefly arrested attention. Cullen, for example, placed the disease among spasmodic neuroses, and it cannot excite surprise that physicians less learned and accurate than he should have seized upon partial aspects of it to name, class, and describe it, thus creating difficulties of identification. It seems certain, however, that Portuguese, Dutch and English physicians found the disease prevailing in India and its dependencies in the fifteenth, sixteenth, seventeenth, and eighteenth centuries; and when the outbreak of 1817 occurred it was recognised as a severe manifestation of a familiar scourge. Since 1817 Asiatic cholera has been watched with keen interest wherever it has prevailed; and the facts relating to its prevalence in India and elsewhere have been recorded with great minuteness and care. Voluminous as these records are, the story of cholera is a very simple and singularly interesting one. It presents the pictures of a deadly disease prevailing perennially in certain parts of India, which have been recognised as its home or field of endemic lodgment, where it waxes and wanes, but never altogether disappears; and of a dread epidemic taking its departure from its endemic habitat, after a recrudescence of more than usual severity, and diffusing itself along the ordinary routes of commerce and pilgrimage throughout the inhabited world. The history of cholera is thus a tale of repeated invasions, presenting a remarkable similarity. It is not easy to define with exactitude the endemic centre from which these invasions have proceeded: some authorities assert that there are several such centres in India; the principal one is undoubtedly the delta of the Ganges and the vast creek and river-netted alluvial plain which lies south of its confluence with the Brahmaputra. How far the endemic area extends up the Gangetic and Assam valleys it is difficult to say; or whether other deltaic regions in India, as of the Godaveri and Kaveri rivers, are also endemic areas. It is important to note that, even in its endemic haunts, cholera presents most of the features which characterise its epidemic facies. It rises and falls, and travels; and if we carefully study particular tracts of country, we shall find that the disease presents a succession of outbreaks and an aspect of grouping very similar to what is observed in Europe when the disease visits a susceptible place and people in a favourable season.

It is observable that every departure of cholera beyond Indian limits has been preceded by an outbreak in India of marked and unusual violence. Its westward diffusions have naturally attracted most attention; but eastern diffusions have also occurred — to the Straits Settlements, Siam, China and Japan — which have not been so carefully investigated. The western invasions have taken place by three routes, namely, (1) through Afghanistan, Persia and Central Asia, to Eastern Russia, along trade routes crossing or bordering the Caspian Sea, and thence into the interior of Russia along the Volga; (2) by the Persian Gulf to Turkish Arabia and Persia; thence to Turkey in Asia, and along or across the Black Sea to Constantinople and the Danube; and (3) by the Indian Ocean and Red Sea to Aden and Mecca, thence to Egypt and the countries bordering the Mediterranean. The disease prefers a land route to a sea route, and has sometimes travelled westwards by more than one route.

Seven distinct invasions of Europe have taken place in the present century. The outbreak of 1817 reached, but did not enter Europe. It covered India in 1818; found its way to Mauritius and Burmah in 1819, reached Arabia, Siam, Malacca, and China in 1820, prevailed in Persia and Asiatic Turkey in 1821, and got as far as Tiflis and Astrakhan in 1823. There its westward march ended.

The first European invasion covers a period of thirteen years — 1826–39. During the first three years India was extensively overrun by it; in 1829 the disease was carried by the Central Asian route through Kabul, Herat, Bokhara, Khiva, and Orenburgh, as far as Nijni-Novgorod; in 1830 it travelled through Persia and by Resht, Tabriz, Tiflis, and Astrakhan to Southern Russia, eventually reaching Moscow. Russia and Poland were then occupied, and in 1831 Northern and Central Europe; in 1832 it invaded the United Kingdom and America, and in 1833 France, Spain, and Portugal; in 1834 Italy and North Africa suffered, and the disease lingered in Europe till 1839.

The second European invasion commenced in 1840 and ended in 1851 — eleven years. Cholera was carried to China by our troops, and after raging severely in that empire, was conveyed by trade routes into Burmah, Yarkand Turkestan, and other parts of the Central Asian plateau. It broke out in Persia in 1845, in Arabia and Turkish Arabia in 1846, it reached Eastern Russia in 1847, and in 1848 it spread through Europe, visiting the United Kingdom, and reaching America *via* New Orleans from Havre. This epidemic subsided in 1851.

The third European invasion covered nine years — 1848–57. It is thought by some authorities to have been a recrudescence of the cholera of 1840–51. During 1848–50 the disease ravaged India extensively; in 1851–52 it spread through Turkish Arabia and Persia, and reached Russia; in 1853 Asiatic Turkey and Northern Europe suffered; in 1854–55 the rest of Europe, Great Britain, and America were invaded. This outbreak, which died out in 1856–57, was the cholora from which the army of the Crimea suffered; and it was during this epidemic that

certain celebrated observations were made upon the agency of water in cholera diffusion.

The fourth European invasion of 1863–67 took place through Arabia and Egypt as well as by way of Persia, the Black Sea, and the Caspian. The disease occupied Europe in 1865, and in 1866 it prevailed in Britain and America.

The fifth European invasion commenced in India in 1867 — the year of the celebrated Hurdwar outbreak — and lasted till 1873. Europe was reached by the Persian and Turkish-Arabian route, and during the years 1870–73 the disease raged in Europe and also in America, which was reached through New Orleans from Jamaica.

The sixth European invasion, dating from 1879, took place *via* Mecca (1882) and Egypt (1883). The countries bordering the Mediterranean suffered first and most, and the disease lingered in these till 1887. Indeed an outbreak in Paris in 1892 is considered to have been a survival of this epidemic. It was in Egypt, in 1883, that Koch discovered the bacillus which has formed so prominent a feature of cholera research in recent years.

The seventh European invasion of 1891–95 is remarkable for the unprecedented rapidity with which the disease travelled westward and overspread Europe. Beginning in Bengal in 1891, it raged in Upper India in 1892, and in the same year ravaged Kashmir and Kabul, travelling rapidly through Persia and Central Asia, and spreading over Northern and Central Europe. There was a violent outbreak at Hamburg, which has so frequently endured severe visitations. Cases occurred in English seaport towns, but the epidemic did not penetrate inland. In 1893 sharp outbreaks occurred at Hull, Grimsby and Yarmouth, and in many adjoining inland localities; but this country as a whole escaped.

From this cursory sketch it is evident that human intercourse and agency are the cardinal factors in cholera propagation: and the main question which has agitated the public mind, and engaged the attention of conferences and commissioners during these years, is whether the progress of cholera can be stayed by stopping communication between infected and non-infected places by means of a system of quarantine. This question resolves itself into two subsidiary questions, namely, whether quarantine be feasible and effective; and, if so, whether the disturbance of social life and interruption of commerce which it implies be justifiable. Unfortunately these questions have been chiefly debated on theoretical grounds, and have mainly turned on whether the disease be personally communicable or the reverse. Sufficient experience has now been gained to render a solution of the question possible on the surer basis of natural experiment. As regards inland quarantine, the experience gained by numerous trials in India and Europe has resulted in almost uniform failure; and when the difficulties of imposing a rigid quarantine and the chances of evasion are considered, together with the possibility that dissemination may be effected by other agencies than human —

by animals, birds, and insects, or by wind and water — it is not strange that the disease has so often overstepped the most rigid cordons. Maritime quarantine presents easier postulates, and has been attended with more success; but ships, unless crowded with emigrants, pilgrims, or soldiers under unsanitary conditions, are not such good porters of cholera as caravans, armies, hordes of pilgrims, and unsavoury travellers by road and rail. The policy of detaining masses of men in unwholesome lazarettos, subject to infection by new arrivals, has certainly proved disastrous; and a system of accurate and early information, careful inspection, isolation of the sick and suspected, and sanitation general and special, has been productive of greater benefit than any wholesale attempt to hinder the movements of men and merchandise.

There are certain parts of the earth's surface, more or less insulated, which have not been visited by cholera. The most remarkable are the Andaman Islands in the Bay of Bengal, Réunion, Australia, New Zealand, and other islands of the Pacific, the Cape of Good Hope and West Coast of Africa, St. Helena, Ascension, the Azores, Bermudas, West Coast of South America, Orkney and Shetland Islands, Iceland and the Faroe Islands. This list is, moreover, by no means exhaustive. There are certain localities in all countries which have seldom or never been visited, while epidemics have prevailed around; and in any outbreak even in India, the places and persons attacked are always a minority of the whole. Even in Calcutta, the head centre and perpetual home of cholera, there is a quarter of the city which possesses as complete an immunity from the disease as Iceland. No better illustration than this could be given of the power of sanitation to extirpate cholera.

Cholera literature is immensely voluminous, and from time to time many theories have been advanced to explain the nature, origin and diffusion of the disease. These speculations, putting aside the purely mythical, have concerned themselves with every possible influence — cosmic, sidereal, telluric, climatic, septic, ochlotic, etc. — to account for cholera visitations. A study of statistical aggregates and too exclusive an attention to "broad" views have begotten vague and fatalistic generalisations, as of mysterious forces and pandemic waves, which have of late years become discredited. General causes do not produce exceptional, limited, erratic, and contingent results; and a closer study of cholera on a more rational basis has made it clear that so specific a malady must have a specific cause. The microbic agents investigated by Koch and others have now for eleven years been subject to criticism, experiment, and research, and year by year his theory has gained support from clinical, pathological, bacteriological, and epidemiological studies. The theory which offers a key to the bewildering mass of cholera literature which the present century has produced, is that which finds the causation of cholera in a disregard of the laws of health, and in the presence of an organic (microbic) poison, capable of conveyance under favouring circumstances by man himself.

K. M.

Etiology and Epidemiology. — Seeing, then, that cholera is due to a living contagium — Koch's cholera bacillus — which, growing in the intestines of the patient, causes death partly by the effect of the toxins produced by it and partly by the profuse purging which it sets up, the further etiology of the disease resolves itself into two factors: first, the means by which the microbe gains access to the body; second, the conditions which render the body susceptible to the microbe. Of the first of these we know much, of the second little.

Mode of Access. — It is certain that cholera is not contagious in the ordinary sense of the word. Cholera cannot be caught by contact, and although nurses and those who attend to the sick are often affected in larger proportion than others, this is readily explained by the fact, that unless constant care is exercised in regard to cleanliness of hands and utensils they are much more exposed than are others to the known and recognised mode of infection, which is by the mouth. All evidence goes to show that the infection of cholera to take effect must be swallowed.

Now, as in all zymotic diseases, the *materies morbi* — the *contagium vivum* — greatly increases within the body of the patient during the progress of his malady. During the disease a minute amount of infectious material grows into an amount capable of giving the infection to thousands; and, in the case of cholera, this infectious material finds its exit from the patient's body in the discharges caused by the disease.

The study of the etiology of cholera, then, is to a large extent a study of the steps by which matter which has left one patient so gains access to some article of food as to be swallowed by some one else.

It is conceivable that in the presence of a great abundance of the infection it might be inhaled in the form of dust. Of this, however, there is no evidence, nor is it probable unless it be in the case of those who have slept in cholera-soiled bedding; the cholera bacillus is so readily killed by desiccation that such a mode of transference is in the highest degree unlikely. It is with food and drink that it commonly gains access to the human body.

Well-authenticated instances are related in which flies have appeared to carry the infection from cholera dejecta to milk and various articles of diet; and M. Haffkine has detected cholera bacilli in specimens of sterilised milk, exposed in new vessels, to which flies were permitted free access during an outbreak of cholera (1).

The use of cholera-infected water for washing cooking utensils and articles used in the preparation of food is another mode of local distribution; especially in regard to the spread of the disease by milk.

In the case of nurses and those who attend to the sick, or have charge of the dead, the cholera poison may, as a result of want of strict cleanliness, be transferred to the mouth by the fingers, either directly or by means of the food they touch.

But the great, the persistent, and the almost universal mode by which the cholera germ gains access to the body is in the drinking water. This is now so well recognised that it is unnecessary to go again over

the evidence by which the fact has been proved to demonstration. It may, however, be well to refer to a few of the classical examples of this mode of cholera distribution.[1]

A full account of the case of the Broad Street pump, which was investigated by Dr. Snow, is to be found in the *Report of the Committee for Scientific Inquiries into the Cholera of* 1854. The relation between the incidence of cholera and the source of the water-supply to different parts of London is described in the *Report of the Royal Commission on Water-Supply*, 1869. The outbreak of cholera in the East End of London in 1866, which was traced to the supply of specifically contaminated water, is described by Mr. Netten Radcliffe in the *Report of the Medical Officer to the Local Government Board*, 1866; and the great outbreak of cholera in Hamburg is described with full statistical detail in the *Report of the Medical Officer to the Local Government Board*, 1892–93.

There is a good deal of evidence to show that water does not act as a mere diluent and distributor of the cholera poison, but that under certain conditions the cholera bacilli grow and for a short time increase in virulence during their sojourn in this medium. In the presence, however, of sunlight and ordinary water-bacteria they are either rapidly destroyed or soon cease to multiply. The persistence of cholera in a district is indicative of more than a single pollution of the water-supply, and generally points to a persistence of some insanitary conditions which favour repeated infection.

It is not always the case, however, that the infection is conveyed directly from man to man by means of water. Where we find sudden outbursts of disease affecting large numbers of people drawing their water-supply from a common source, some direct and wholesale fouling of the supply is generally the cause of the mischief. But much more commonly, especially near its endemic home in India, cholera does not occur in great outbursts; small local epidemics arise, die down, and then recur. The cholera bacillus, in fact, grows in the foul soil, is now and again washed into the wells, and so sets up disease in those that draw their water from them. The key, then, to this side of the etiology of cholera is to be found in the habits of the people, and the degree of care or want of care they exercise in the protection of their water-supplies.

The natural home of cholera is a land of foul water. In Lower Bengal, where cases are reported every month in every year, an inquiry into the habits of the people, and the condition of the tanks from which they largely draw their water-supply, is sufficient to show how constant are the opportunities both for food and water, especially the latter, to be exposed to fæcal contamination.

In many of the towns of Southern Europe, also, which have most markedly suffered from the ravages of cholera (among these Naples and Marseilles may be specially mentioned), it has been demonstrated that

[1] In how wide a sense the term "drinking water" may properly be applied is indicated by the alleged dissemination of the cholera poison by means of oysters which had been exposed to the affluence of sewage.

while the water-supplies had been contaminated, the habits of the people had intensified the evils resulting from this cause. On the other hand, our own practical immunity during the epidemics which have broken out in Europe since greater attention has been given in England to the securing of pure water, compared with our great mortality from cholera in earlier epidemics, together with the great lessening of the cholera mortality in those towns in India which have obtained pure water while epidemics have continued as of old in surrounding districts, both tend to show that when the habit of drinking water which has been exposed to chances of fæcal defilement is once broken cholera fails to take root.

Individual Susceptibility.— We do not, however, completely explain the etiology of cholera by the statement that it depends on the ingestion of cholera-infected water; another condition is also necessary, namely, the susceptibility of the individual.

Considerable differences exist in the habits of the various members of every community; thus it often happens that even where the habits of the majority are foul, a few are protected from receiving the infection by the greater cleanliness and propriety of their lives. Yet many fail to sicken, although they are known to have swallowed the very infective matter which at the same time is producing cholera in others. We have proof of this in every wide-spread water epidemic; the number of those who swallow the poison must in these cases vastly exceed the number of those who are attacked by the disease. Macnamara gives an instance in which a vessel of drinking water was accidentally polluted with fresh cholera excreta, and after being exposed to the sun all day the water was partaken of by nineteen persons; of these five only subsequently suffered from cholera.

It seems clear that the inhabitants of the areas in which cholera is frequently present, notwithstanding habits which expose them continually to chances of infection, are much less frequently attacked than new arrivals in the districts, much less, for instance, than Europeans, although when attacked they succumb more readily. How far this immunity is racial, or how far it is the result of a frequently repeated small infection, creating and maintaining an artificial immunity (as is presumed by some to occur in the case of yellow fever), is a question which cannot at present be decided. There is, however, much in the progress and rapid recession of cholera epidemics to favour the opinion, that exposure to the influence, if it does not produce the disease, does induce some temporary immunity.

On the other hand there is a good deal of clinical evidence — of a nature, however, that can hardly be brought to the test of statistics — to show that any disturbance of the balance of the digestive organs, especially the dyspepsia common among drinkers, and the looseness of the bowels often brought on by eating over-ripe or decomposing fruit, distinctly tends to leave the patient open to the cholera infection — that in fact an active gastric digestion and a healthy intestinal mucous surface form a considerable bar to attacks of cholera.

The predisposing influence of poverty and bad food partly consists, no doubt, in such disturbances of the digestive organs; while the thirst and consequent ingestion of large quantities of water common among the labouring people may cause indigestion, and do expose them to increased risks of cholera when the water is infected.

So far we have considered the etiology of cholera as it affects the individual. We have shown that although the condition of the patient has an influence on the effect of the attack, the immediate factor in the production of cholera is the swallowing of an infection which has come, directly or indirectly, from the dejecta passed by another patient suffering from the same disease; thus we have demonstrated that cholera may properly be called a filth disease: not that filth, unless infected with cholera, can cause the disease, but that, without the filthy habits which bring about the consumption of food or drink befouled by man's dejecta, cholera cannot be transmitted.

Epidemic Prevalence. — This view, however, of the etiology of cholera by no means explains the occurrence of epidemics, nor the tendency of these epidemics at varying periods to spread beyond the normal confines of the disease, to extend into areas which for long series of years had been entirely free from it, to advance stage by stage, and thus to march around the globe; then to retire, and for an uncertain period either to lie latent or to be confined within the endemic area.

To understand this peculiarity of cholera, it is necessary to bear in mind the various factors which aid in the dissemination of the disease, and to recognise that it is the coincidence of many factors which sets cholera on the march.

Within certain areas in India cholera is endemic, especially in the country of the Lower Ganges. There "the air, the water, and the soil are never cold, the ground is often damp, and when it is dry the tanks are foul, so that there is always a fit breeding-place for the contagion, and the habits of the people in every way facilitate its entry into their systems"(2).

The habits of the people and the condition of the water-supply in many Indian villages are such that, if one did not bear in mind that a necessary factor in the etiology of cholera is the susceptibility of the individual, one might expect the whole mass of the inhabitants to perish rapidly of that disease. If, however, we examine more carefully the incidence of cholera within the endemic area, it becomes obvious that, although in every district deaths from it may be reported every year and every month in every year, still the incidence of this mortality is by no means evenly distributed; even within the endemic area cholera wanders about, one village after another being attacked and then left at peace for a time. It seems as if there were the same tendency for these outbursts to die down within the area as there is outside it; but that in consequence of the great facilities for reimportation, and of the condition of the soil, which makes it possible for the germ to maintain its vitality and carry on the saprophytic phase of its existence for a considerable time, the

disease frequently crops up again — whenever, in fact, there is a sufficiency of susceptible people for it to prey upon, and whenever accident introduces it afresh into the drinking water.

It is important to bear in mind the somewhat curious fact, that the highest mortality from cholera does not occur in the parts in which the disease is permanently endemic; this points strongly to the probability that dwellers within the endemic area attain some degree of immunity from the infection.

The Spread of Epidemic Cholera. — One of the most striking peculiarities of epidemic cholera, when it oversteps the bounds of its endemic area, is its tendency to advance along fairly definite tracks; to go from town to town, from country to country; to attack each fresh district with enormous virulence at first; then, in a short time, to become much modified in intensity, subsiding altogether in about three months to return again the next year, and perhaps the year after; then again to die out entirely till it is introduced afresh, passing on meanwhile to some other place where the same course is repeated. The study of the epidemiology of cholera thus involves that of the modes by which the disease is carried from place to place, the influences which favour its dissemination, those which favour or retard its taking root in fresh localities, together with those curious periodic variations of intensity which, for the sake of a phrase, are sometimes attributed to "epidemic influence."

There can no longer be any doubt that cholera is disseminated by human intercourse. The march of cholera coincides with the march of man, and it is carried from place to place either by infected man or by cholera-tainted clothing. There seems no practical limit to the distance to which it would be possible to transmit the infection in a bundle of imperfectly dried rags soiled by cholera excreta; man, however, can but carry the disease so far as he is able to travel between receiving the infection and being laid low.

What we find, then, on comparing the march of the earlier epidemics of cholera with those that have occurred in more recent years, is that whereas when travel was slow the disease swept steadily forwards, occupying the land as it advanced; in later times it has bounded forward with long strides, occupying outposts far ahead of infected areas by means of railway and steamboat communication, and then, from these outlying foci of infection, has spread in both directions, coalescing perhaps at a much later date with the main body of the epidemic which has slowly advanced across country from the earlier centres.

Certain as it is, however, that man is the porter by whom cholera is introduced to any place, it must not be forgotten that its development in that place depends on insanitary circumstances, the chief condition necessary being the liability of the drinking water to be contaminated by infected excreta. Hence it has happened again and again that cholera has proved the touchstone to the sanitary deficiencies of towns and districts, leaving unharmed those with pure water, and ravaging those whose water-supply was open to defilement.

It will thus be readily understood why cholera is so apt to be spread in epidemic form by wars and pilgrimages. Cholera may and often does travel along the tracks of ordinary trade; but it never advances far unless along its path there be places where the sanitary conditions enable the disease to take root and start upon its course afresh. When, however, as in the case of wars or pilgrimages, great bodies of men are camped out without any proper means of dealing with their excreta, or any assurance that their water-supply remains untainted; and especially when, as is the case in the great religious pilgrimages which are recruited from within the endemic home of cholera, the men who form these camps carry with them those habits and customs which, within that area tend to make cholera permanently endemic, then we find every condition fulfilled for the epidemic propagation of the disease.

Accepting the view that when cholera is introduced into new districts it is carried thither by cholera-infected rags, cholera-infected food, or cholera-infected man, it becomes a matter of great importance to determine whether the last (namely, cholera-infected man) can carry with him the germs, deposit them in fresh places, infect water-supplies, and set up epidemics, without himself suffering from cholera and betraying its symptoms. Till a few years ago this question would have been unhesitatingly answered in the negative; and in fact it is in the belief that a man cannot carry cholera unless he himself suffers from it that the modern substitute for quarantine is founded, namely, the system of medical inspection and detention of invalids. Modern travel is conducted on so vast a scale, and the numbers moving from place to place are so enormous, that efficient quarantine is obviously impossible. It has been hoped, however, that if those actually ailing be sorted out the rest may safely be allowed to pass. Hence the modern system. The more recent investigations of Koch and others tend, however, to throw some doubt upon the efficiency of such measures; and although they have appeared successful in preventing the disease from taking root in England, it is quite possible that the greater attention which of late years has been given to the purity of the water-supply of our towns may have had a much larger share than our port sanitary inspection in giving us the exemption we have enjoyed. Koch has shown (3), and it has been shown repeatedly at the observation stations which were established in Germany at the time of the epidemics in Hamburg in 1892 and 1893, that among those who had been exposed to the possibility of cholera infection, and who yet remained apparently healthy, there were individuals whose fæces although hardly diarrhœic — nay, quite normal — yet, nevertheless, contained cholera-bacteria. "It is now certain that among a number of persons who have been exposed to cholera infection the resultant cases may show the whole scale from the severest and rapidly fatal cases down to the mildest imaginable, demonstrable only by bacteriological investigation."

The determination of this point goes far to explain outbreaks of cholera in which the first apparent sufferers could be shown not to have

entered any infected district. The very first case has, in fact, not been recognised, maybe the patient has not known that he was ill; his dejecta have nevertheless obtained access to the water-supply, and thus given rise to the outbreak. It seems only in this way possible to explain some of the isolated sporadic cases which have occurred in England, cases in which, notwithstanding the entire want of evidence of any connection with any known focus of the disease, the typical micro-organisms have been discovered.

Conditions determining Character of Outbreak. — When the cholera germs have once been introduced into a district their fate will depend on various conditions. If they chance to gain access to a public water-supply they will, as has been shown again and again, set up a sudden and wide-spread epidemic among the consumers of the water — an epidemic which breaks out simultaneously in different parts of the district, rages violently for a time, and if the infected water be cut off, stops almost as suddenly as it had begun.

If, however, the germs do not gain access to a general water-supply, but are deposited in the neighbourhood of the dwellings of the people, they will only set up small and localised outbreaks; in one part after another of a town, in one town after another, cholera will arise and soon die out, only to crop up again in neighbouring places, or even in the same place again; and thus an epidemic, never perhaps severe, may continue so long as to cause serious loss of life. The continuance of an outbreak of this latter sort depends upon local conditions; and it is obvious that, although a general water-epidemic has a sudden rise and a sudden fall, one occurring in a district which favours the development of foci of cholera, although it may rise as suddenly, will not terminate so quickly: it will rather set up a multitude of centres from which it will continue to spread as in the second mode, the mode in which it mostly shows itself in countries in which it is endemic during non-epidemic times — countries in most parts of which no such thing as a public water-supply, in the modern sense of the term, exists. It becomes then very important to inquire into the causes other than the infection of public water-supplies which favour the development of epidemic cholera; for it is certain that "in many districts of greater or less extent, the cholera has never reached any considerable or strictly epidemic development notwithstanding repeated importations of the poison" (4).

Conditions favouring the Development of Cholera Epidemics. — Hirsch says, "As there are certain local peculiarities which furnish the conditions for the endemic disease, so also there are certain factors residing in the circumstances of place or season, which are necessary to give potency to the cholera poison beyond its native habitat;" and he quotes Hergt as saying, "The rise of the cholera epidemic at any one place implies, besides importation of the contagium, certain local conditions of atmosphere and of soil as well. These conditions must be able at a given place to generate themselves and to disappear again." The latter is an important qualification, for it appears certain that

among the causes necessary for the development of cholera in an epidemic form, except when widely distributed by water, are some which are purely temporary, as for example those which are connected with season; and that a locality, which at one time may be capable of developing cholera in a most virulent form, may at other times be, comparatively speaking, protected from its attacks. Putting then on one side infection of public water-supply, which is capable of creating an epidemic in any place and in any season, we have to consider the factors in the production of an epidemic not arising from that cause.

According to Dr. Davidson (6) they may be classed as — Local conditions: Seasonal influences: Predisposing conditions: Facilities of intercourse: Race proclivities: Epidemic influences.

Of these the "predisposing conditions" and the "racial proclivities" have already been dealt with; and after what has been said regarding the mode of dissemination of cholera, the importance of facilities for intercourse is obvious. "Epidemic influence," again, and the curious tendency of cholera, like other infectious diseases, to rise into epidemic importance at moderately regular intervals of time, must be regarded as due to the coincidence of several causes, each emphasising the importance of the other. It remains then to consider the conditions of place and of season which influence the occurrence of epidemic cholera.

(*a*) Altitude. — Elevated districts often remain exempt from cholera; on the other hand valleys and low-lying areas are much more apt to suffer: in towns situated on a slope, or occupying different elevations, it is usually found that within the same town the higher districts are least affected. On the other hand, cholera has occurred at very considerable altitudes, and even sufficiently often in the higher parts of towns to make it clear that the cause of the apparent variation of cholera with altitude must be sought elsewhere, probably in its relation to temperature, water-supply, and movement of ground water.

(*b*) Relation to Rivers. — It has constantly been observed that not only does cholera follow rivers, which it should be noted are also commonly lines of traffic and centres for the aggregation of large populations, — two main factors in the dissemination of the disease, — but that it attacks places on the banks of rivers and even of small streams with special severity. This again probably has relation to conditions of soil and density of population, as well as to the double function of rivers as drains and sources of water-supply.

(*c*) Character of Soil. — Cholera attains its greatest intensity on soils which are permeable to water, but not sodden with it, and are at the same time capable of retaining a certain degree of moisture within their interstices.

The relation then of altitude, neighbourhood of rivers, and character of soil may all resolve themselves into this — that cholera is most likely to take on its epidemic character on a soil which is porous, more or less charged with decomposing organic matter, moistened with water, and having its interstices filled with air. On such a soil complete dryness, as

was seen in the famine districts in India, or complete saturation as is seen in the rainy season in certain districts, are inimical to cholera: while a falling ground water, leaving the soil moist, full of air, and charged with organic matter from the surface, disposes to cholera; not only by favouring the saprophytic growth of the cholera bacillus, but also by facilitating its access to wells.

(*d*) Seasons and Weathers. — In like manner the influences of season and of weather can be reduced to those of temperature and rainfall. A certain temperature is necessary for the development of the cholera bacillus outside the body; but cholera is not always most prevalent in the hottest weather, nor is it always stopped by winter. It seems probable, however, that in those cases in which cholera has occurred in winter there has either been a direct infection of a water-supply, as in the case of the outbreak at Nietleben in January 1893, described by Koch (7), or the infection has gained access to the soil under houses which, as in Russia, have been kept continually at a high temperature, and has thus reached the drinking water indirectly. In temperate climates the great mortality from cholera takes place in the warm weather; in England August and September are the most fatal months. In India, however, the greatest prevalence of cholera is by no means synchronous in the different parts of the country, nor does it uniformly accord either with greatest heat or with the maximum or minimum of rainfall. Along with heat there must be moisture of soil for cholera to prevail. On the other hand the soil must not be sodden with water, as in some places is the case in the rainy season; thus it happens that in some districts with dry soil the rains by introducing the moisture necessary for its development and by washing the infection into the water-supply, seem to bring cholera; while in other districts, in which there is usually a certain moisture of soil, the rains will stop an epidemic by filling up the pores and removing the aeration of the soil necessary for the continuance of the saprophytic growth of the bacillus. Heat, moisture, aeration, and the presence of decomposing organic matter in the soil are then the conditions favourable to the local development of cholera when once introduced; and the more of these conditions which coincide in any place and time the more likely is cholera in its epidemic form to prevail at that time and place.

(*e*) Habits of Inhabitants. — Even amidst the conditions of soil and climate most favourable or most inimical to cholera, its prevalence largely depends upon the habits of the people; however largely present its contagium may be it is harmless unless swallowed. Thus among all the influences making for cholera, the most important are those habits of carelessness as to the cleanliness of food and drink which make it easy for either the one or the other to be tainted with fæcal material.

(*f*) General Sanitation. — As is the influence of the habit of cleanly living to the individual, so is that of general sanitation to the body corporate. Good drainage and good water-supply keep cholera at bay by making it impossible for the fæces of one person to gain access to the drink or food of another.

This brings us back to the key-note of the etiology and epidemiology of cholera, namely, the ingestion of infected water or infected food.

The act of swallowing the living contagium derived from the excreta of a previous sufferer from the disease is the immediate cause of cholera in the individual; while the means by which facilities are given for the growth of this contagium outside the body, for its wide-spread dissemination, and for its introduction into the food or drink of man, are the causes of cholera epidemics.

Ernest Hart.
Solomon Charles Smith.

Bacteriology of Cholera

It is a difficult task to give a comprehensive and impartial sketch of the bacteriology of cholera. Opinions have constantly changed since Koch's discovery of the comma bacillus, and from the very outset his conclusions have been strongly opposed. More recent experience has led to changes of opinion, and, however impartial our endeavour, we cannot at present find a satisfactory solution of the matter. We shall do our best to present it in a more or less historical order. In this conflict of opinions there are two distinct periods: the first, dating from Koch's discovery of the comma bacillus in 1883 until the recent appearance of cholera in Europe; and the second, beginning with the cholera epidemic in 1892. During the first period Koch was the central figure, and the study of the cholera organism was more or less restricted to laboratory research: on account of the scarcity of choleric material general criticism was impossible. On the return of cholera to Europe pathologists and bacteriologists were enabled to make independent observations, and a general exchange of opinions became possible.

First Period 1883-1892. — In 1883 Koch separated a characteristic curved organism from the dejecta and intestines of cholera patients, the comma bacillus; this he declared to be absent from the stools and intestinal contents of healthy persons, and of persons suffering from other affections. The organism was said to possess certain morphological and biological features which readily distinguish it from all previously described organisms. It was absent from the blood and viscera, and was found only in the intestines; and in the greater number, it was said, the more acute the attack. Koch also demonstrated an invasion of the mucosa and its glands by the comma bacilli. The organisms were found in the stools on staining the mucous flakes or the fluid with methylene blue or fuchsin, — and sometimes alone: by means of cultivation on gelatine they were readily separated from the stools. During his stay in India, in Egypt, and at Toulon, Koch had examined more than a hundred cases, and other investigators confirmed his statements. Numerous control observations, made upon other diarrhœic dejecta and upon normal stools, were negative; the comma bacillus was found in choleric material only, or in material contaminated by cholera. Soon other observers, however,

described comma-shaped organisms of non-choleraic origin; Finkler and Prior, for instance, found them in the diarrhœic stools of cholera nostras, Deneke in cheese, Lewis and Miller in saliva. All of these organisms, however, differed in many respects from Koch's comma bacillus; and gradually the exclusive association of Koch's vibrio with cholera became almost generally acknowledged. In 1886, indeed, Flügge maintained that the comma bacilli must be regarded as the cause of cholera, because they occur constantly and exclusively in this disease.

Koch described his vibrios as short, curved organisms, often arranged as spirals; the curvature of the individuals varies greatly, the latter being sometimes almost straight, and at other times nearly semicircular. Two commas may be attached so as to form an S; spirals, even of great length, may indeed be found. They possess the power of spontaneous movement in a marked degree, and readily undergo involution, becoming round and coccoid or irregular in appearance. Hüppe assumed these coccoid forms to be arthrospores; his observations, however, are by no means convincing.

On the surface of a gelatine plate the growth, as described by Koch, is characteristic during the early stages, the colonies appearing as small, whitish, refractive points, so that the gelatine seems to be sprinkled over with delicate glass splinters; as the liquefaction of the nutrient medium progresses this appearance is lost. Stab-cultures in gelatine are equally characteristic: there is a whitish growth along the needle-track with gradual liquefaction, which at first is most marked near the surface, so that a funnel-shaped depression is formed which appears to contain an air-bubble. Liquefaction is comparatively slow, but after six days it has progressed so far as to destroy the appearance just described. On agar-agar we have a superficial slimy growth, offering no special features; growth occurs on potato at a raised temperature only; milk is not coagulated. Koch's vibrio is capable of thriving in very dilute broth or peptone solution; it is a facultative anaerobe, and grows best between 30° and 35° C.; drying, acids, and most disinfectant solutions destroy it quickly.

Animal experiments, in so far as their aim was to reproduce a typical choleraic lesion, were not successful in Koch's hands; nor can those performed by Nicati, Rietsch, and Van Ermengem be considered convincing. Subcutaneous inoculations and feeding led to no result; direct inoculation into the duodenum, with or without previous ligature of the bile duct, frequently produced fatal diarrhœa with abundant vibrios in the dejecta, but since this result seemed to depend to a great extent on intestinal injury they are not free from doubt. Koch himself, indeed, asserted that he had induced a choleraic process by feeding guinea-pigs with pure cultures, after previous neutralisation of the gastric contents and injection of tincture of opium into the peritoneal cavity, in order to paralyse the intestinal peristalsis. Yet as other vibrios act in the same manner these animal experiments have not established the specifically pathogenetic power of the comma bacillus. The sterile products of choleraic cultures administered to a guinea-pig will cause distinct intoxicative symptoms

or death, as first shown by Nicati and Rietsch; these symptoms, however, do not differ from those produced by many other bacterial toxins. We shall refer to human experiments later.

Löffler demonstrated that the cholera vibrio possesses a single terminal flagellum, but others have shown that it may possess more than one. Of more interest, however, is a peculiar chemical reaction which Koch pronounced to be characteristic, the so-called cholera-red reaction. On adding pure hydrochloric or sulphuric acid to a culture in peptone solution or in peptone broth, a pink or red colour (cholera-red) appears. This reaction was discovered by Pöhl, Bujwid, and Dunham in 1886 and 1887, and was explained by Salkowski, who at the same time proved it to be of no specific value. It depends merely on the formation of indol from the albuminous substances in the culture medium. Many organisms give the same reaction: some on the addition of nitrites, others without this addition; the latter possess the power of converting the nitrates contained in the broth or peptone into nitrites first. This the cholera vibrio can do, but many other vibrios and bacilli do likewise.

This short description of Koch's comma bacillus must suffice. He considered it to be the one specific cause of cholera, and to be constant in its characters: any vibrio which did not agree in its features with the one discovered by himself was at once put aside as non-choleraic. This ban fell upon the various vibrios described by Finkler-Prior, Deneke, Gamaleia (vibrio Metschnicovi), and others.

The specific germs — Koch's comma bacilli — are shed in the stools from the body during the first days of the disease; and only these, or matter contaminated by them, as for instance the bed linen, vessels, latrines, soil or drinking water, can be sources of infection. Since the vibrio is readily destroyed by drying, only freshly-contaminated objects are dangerous. Yet it has been shown that the vibrio, when kept moist, may retain its vitality for a considerable time. It follows, therefore, that the disease to be carried from an endemic area must either be uninterruptedly transmitted from one individual to another, or must pass by a general source of infection, as for instance a contaminated water-supply. Aerial infection is excluded; hence there must be either direct contact with choleraic material or the consumption of contaminated food or unclean water. Moreover, some personal disposition, brought about perhaps by dyspeptic conditions, or by the general debility of poverty, starvation, and overcrowding, may or must co-operate with the specific agent. Nor are locality and season without moment. In some localities the disease seems never to occur; and the exemption finds an explanation in a difference of water-supply, of hygienic and economic conditions, and is independent of the particular state of the soil. So far as the seasons are concerned, the cholera epidemics in the temperate zones reach their climax during the late summer and in autumn; that is, during those months when insects abound, when raw food is copiously consumed, and when gastric derangements are common. Such in brief is the mechanism of infection as it was explained by the contagionistic school which believed in a single specific cholera vibrio.

Pettenkofer was one of the earliest opponents of this school; and until now he has defended the "localistic" view against those of Koch and the contagionists. He too believed in a transmissible virus (x), but that an epidemic cannot arise without concomitant conditions which depend on differences of locality and season (y); so that, although x alone may cause an individual case, an epidemic can only appear when x and y coincide. Pettenkofer sought and still seeks y more particularly in special conditions of the upper layers of the soil which affect x in such a way as to render it infective. He denied formerly that Koch's bacillus is x, because of its lack of resistance to external influences. Koch's adherents maintained that Pettenkofer's explanation did not apply to cholera epidemics generally, and that the recent outbreaks especially failed to satisfy his conditions. Although Pettenkofer has now accepted Koch's vibrio as the factor x, he still adheres to the unknown y on epidemiological evidence. After the Hamburg epidemic he reminded us that the cholera germs may often remain quiescent, so that the epidemic appearance of cholera depends not so much on the presence of comma bacilli or a personal disposition, as on certain associated states of locality and season. He complains that contagionists do not pause to consider why certain localities and areas are not visited by an epidemic, although sporadic cases of cholera are constantly present in them. He alleges that, in spite of railways and steamers, cholera does not spread quicker or more generally than formerly, and this with him is a strong argument against the contagionist theory. Cholera epidemics, he asserts, appear only in places with a local disposition.

The staunchest opponent of Koch's school has been Dr. D. D. Cunningham, who is not yet reconciled to the opinion that the "comma bacillus" is a specific element. In 1890 he claimed to have demonstrated that several distinct species of vibrio occur in association with cholera in Calcutta, the home of the disease; so that, according to him, no one species, and least of all Koch's which he never found, can be regarded as the cause of the disease. He agreed with Koch that, as regards the vast majority of cases, the presence of large numbers of vibrios in the intestines is characteristic and even diagnostic. But he has seen "undoubted" cases of cholera without comma organisms; and he has further observed that the vibrios separated from other cases were not of one, but of various species: in fact, from sixteen cases he obtained no less than ten distinct species, distinct morphologically, biologically, and chemically. He therefore concluded that Koch's theory of cholera, as primarily due to the access of a specific comma bacillus to the interior of the intestinal tract, must be abandoned; and if comma-shaped organisms are to be regarded as entering into the causation of cholera, it must be as members of a group of various species. In one case he separated three distinct species — a fact which suggested to him that the special morbid condition existing in choleraic enteritis is the cause of the presence of the comma bacilli. Cunningham has followed up his observations for some years, and he is confirmed in his opinion that the vibrios which he found in association

with cholera are not of one kind, nor even varieties of one species, but are of different species. He has continued to cultivate the forms obtained for long periods under equal conditions, and has found that they remain distinct, and that there is no approximation in morphological and biological characters. He states that some of his choleraic vibrios differ from others as much as the organism of Finkler-Prior differs from Koch's comma bacillus, or as the B. subtilis from the anthrax bacillus. As no one regards the latter bacilli as varieties of the same species, there is no justification for regarding the various choleraic vibrios as aberrant forms of a common stock. Cunningham is indeed disinclined to admit that cholera is due to the access of a member of a group of vibrios; he sees in cholera a disease caused by a ptomaine which produces certain changes in the intestinal tract favourable to the growth and development of sundry vibrios.

Until recently Cunningham's views as to the multiplicity of vibrios associated with cholera were either left unnoticed or generally opposed; but Dr. Klein has fully confirmed Cunningham's statements as to the permanently different cultural characters of various forms of choleraic comma bacilli; though he does not discuss their specific affinities. Klein himself, however, until recently, based his doubts as to the causal relation between cholera and Koch's comma bacillus chiefly on animal experiments. He accepted then, as he does now, the fact that vibrios are almost always found in large numbers in cholera; but he considered that experimental proof was wanting. It had been asserted by Koch and his school that comma bacilli, when introduced into the small intestine in a living state, are capable of setting up an acute illness resembling Asiatic cholera. We need not give Klein's arguments in full, because it is now generally acknowledged that the lesions produced in guinea-pigs and other animals by subcutaneous, intraperitoneal or intestinal inoculations have no specific characters, and may be caused by many other organisms besides the so-called cholera vibrio. It is evident, then, that since choleraic symptoms cannot be produced in animals, and since lesions identical with those following on inoculation with choleraic vibrios are called forth by many organisms, the animal experiment cannot be used in support of Koch's thesis. Intraperitoneal inoculations are followed by fatal peritonitis, but this does not differ from that produced by similar inoculations with the bacillus prodigiosus, the vibrio of Finkler-Prior, typhoid germs and other micro-organisms. Nor can it be maintained that the intestinal inoculation has any specific character, for identical phenomena may follow if we use other vibrios, such as the spirilla of Finkler-Prior and of Deneke. According to Klein, then, animal inoculation cannot be said to have proved the causal relation between Koch's vibrio and Asiatic cholera. Klein has always agreed with other observers that vibrios are extremely common, and almost constantly found in the intestinal contents in cholera, although he could not confirm Koch in the assertion that the more acute and severe the case the more numerous are the comma bacilli in the lower ileum; he did not find this definite relation, and indeed the assertion is now generally withdrawn. His attitude has always been

one of reserve, which is justifiable, and indeed imperative, so long as the chain of evidence is incomplete.

Second Period. — The second period is characterised by energetic investigation of the morphology, biology, and etiological importance of the cholera vibrios. It soon became evident that from stools derived from cases clinically recognised as cholera various forms of curved micro-organisms can be obtained, which morphologically as well as in artificial cultivations often do not even resemble Koch's comma bacillus, and differ greatly one from another, or at least sufficiently so, to raise the suspicion in our minds that in cholera we are dealing with more than one kind of vibrio. Even the unwavering supporters of Koch's views became aware that there is more than a grain of truth in Cunningham's observations on the variability in form. Klein's cholera studies in England, the only complete ones in this country, have clearly shown that several varieties of vibrios are associated with cholera — a point upon which most observers are now agreed. The burning question is whether these forms are merely varieties of one choleraic vibrio, or are different species. If the latter be the case, and we find that the numerous forms associated with cholera are specifically different, one vibrio in particular cannot any longer be regarded as an invariable antecedent. This difficulty has been felt by all who are acquainted with the bacteriology of cholera. These inquirers are now divided into two camps: (1) those who believe with the majority that cholera is due to one organism which may show certain variations — in other words, that cholera is a strictly specific disease; (2) those who contend that, as suppuration may be caused by any one of a certain number of micrococci, so likewise may cholera be caused by more than one vibrio. The present confusion therefore is great, and much ingenuity has been manifested by the adherents of the one view to overthrow the assertions of those who accept the other. As yet we have not reached the solution of the problem.

Those who, amid numerous existing varieties believe in the unity of the choleraic vibrio, employ special tests whereby we may decide whether we are dealing with the specific vibrio or with one resembling it; seeing that a number of vibrios have been found in water or elsewhere, for which places may readily be found in the long series of the varieties of the cholera microbe. Artificial cultivation on ordinary nutrient media, under usual or unusual conditions, has shown that these choleraic vibrios are highly pleomorphic, and that they readily change morphologically and biologically, chemically and physiologically. Thus Dunbar, a firm believer in the vibrionic unity of cholera, admits that typical comma bacilli when kept in water vary and differ more from one another than non-choleraic water vibrios. True vibrios may become so altered as to belie their origin altogether. This extraordinary variability, which readily leads to permanent changes, is a property which must not be left out of sight; it must make us cautious in our criticism, for it is more than probable that what a few test-tube processes can effect nature and disease can do far more thoroughly. The collected observations of the last few

years, if they remove a great part of the force of Cunningham's opposition, have impressed upon us the difficulty of the bacterioscopic diagnosis of the choleraic vibrios. Koch for his diagnosis relied on microscopical preparations, growth in peptone solution, on gelatine and agar-agar plates, on the indol reaction, and on the positive animal experiment; but it was soon found that few, if any, of these tests could be relied upon.

(*a*) Gruber, after patient work, came to the conclusion that the only certain criterion is the appearance of the colonies in a gelatine plate. He points out that the attempts to formulate characteristic differences in the microscopical appearances between Koch's and the other comma bacilli are vain; seeing that one and the same race of Koch's or other vibrio may present morphological characters varying as the conditions of growth and the age of the cultivation. The difference in the microscopical appearance between individual races and cultivations is often greater than that between different species; so that it is impossible by this method to distinguish the cholera vibrio. Gruber admits that the variety of cholera vibrio, first described by Pasquale in an epidemic in Massowah, differs in the most remarkable way from that of Koch. These differences have been maintained for a year and a half in cultivations on various media, and after passing it through the body of animals. Further, the Massowah vibrio possesses from four to six flagella: Koch's generally has one only; but in cover-glass preparations some were always found to possess two or three, so that this feature is not a constant one, and it is possible to regard the Massowah vibrio simply as a variety and not as a distinct species.

For a long time it was considered that the rapidity and manner of liquefaction of gelatine would constitute a simple method of diagnosis. But it was found that the different generations of the cholera vibrio show wide differences in the property of liquefying gelatine; some liquefy it almost as rapidly as does the vibrio of Finkler-Prior, some hardly liquefy it at all: as most of the allied species of vibrios lie within these limits Koch himself has abandoned this test. Gelatine plate cultivations, according to Gruber, are of much more value. Here it is important that the composition of the gelatine should be constant, and that the temperature be kept at or about the same level — 20° to 22° C. being the most suitable. The thickness of the layer of gelatine on the plate, the depth of the colonies, the number of the colonies, the presence of other bacteria, all are factors which influence the appearance of colonies; and, finally, the distinguishing characters of different species only make their appearance at certain stages of development, so that the observation must be repeated at definite intervals of time.

The superficial and the deep colonies of the cholera vibrio differ in appearance. The superficial colonies of Koch's vibrio in 45 to 48 hours old gelatine plates differ from all other known vibrios except Deneke's cheese vibrio: (1) The superficial colonies of the earlier stage present an irregular (never simply round or oval) shape, and have either a coarsely granular or a furrowed or striated appearance; while the colonies of all other vibrios, with the exception of Deneke's, have a rounded shape, and appear

quite structureless, or at most finely striated. (2) The deep-seated colonies, even in sparsely-sown plates, present at an early stage an irregular shape and a wavy, uneven appearance. In the case of old and attenuated cultivations this irregular, uneven appearance may be but slightly marked, yet it is always present.

On the other hand, all other vibrios (excepting Deneke's), especially in thinly-sown plates, appear rounded, quite structureless, and with a smooth surface. On thickly-sown plates the deep and superficial appearances of these colonies present a great similarity to that of the cholera vibrio; so that the difficulties surrounding this procedure are many, and Gruber admits that after all the test is not conclusive.

With certain cholera vibrios these characteristic appearances may be only slightly marked or altogether absent. Thus some cholera vibrios liquefy very slowly, and the superficial colonies have then quite an aberrant appearance — in fact, an appearance so distinct from the classical appearance that one might be tempted to describe two kinds of cholera vibrios simply on the ground of these differences.

Yet further study has convinced Gruber that it is possible by gelatine plates to distinguish all vibrios from that of Koch, except Deneke's vibrio. But seeing that external conditions have so great an influence, and that the variations in mode of growth of a particular species are so great, this method of determining the species, as Gruber admits, is extremely difficult and perhaps uncertain; and seeing that Gruber's test breaks down with Deneke's vibrio, for this reason alone it must be regarded as useless. Recently Gruber himself has confessed that although we know with certainty that the vibrios which are associated with the choleraic processes cause the symptoms and lesions of the disease, yet we cannot diagnose the true nature of these vibrios with like certainty; hence, at present, we cannot definitely state whether those which have been separated from genuine cases of cholera belong to one or several species, or whether they are identical all over the world. The fact which he now also accepts — that copious proliferation of these vibrios may occur in the intestinal tract without leading to serious disease — while it compels him to assume the co-existence of certain unknown factors necessary for the appearance of cholera in the individual or in a locality, renders his position somewhat paradoxical.

(*b*) Pfeiffer, who has never doubted the correctness of Koch's observations and deductions, recognising, nevertheless, that none of the proposed tests vouchsafe a certain diagnosis, introduced a novel method of distinguishing between true and false cholera vibrios. It was based on the fundamental proposition expressed by Behring, that the serum of a protected animal is specific in its action; that is, if injected into an animal it confers on it an immunity only from the lesion against which the original animal had been protected. Pfeiffer, therefore, rendered animals proof against a cholera vibrio, and then used their serum as a test. Its action being specific, it can counteract the effects only of one species of vibrio, and must be impotent against all others. His method of proced-

ure is as follows: he injects a mixture of anticholera serum with the suspected organism: if the animal succumb, the organism in question cannot have been a cholera germ; if the animal survive, our suspicions have been justified. Those who dissent from him object that this argument entirely begs the question as to the true choleraic vibrio. Pfeiffer selected at the outset a comma bacillus obtained from Hamburg, and used it as the genuine form before he had demonstrated its specific value. The dissenters, therefore, refuse to accept his test: it may distinguish between varieties or species, but it does not prove the specific nature of the vibrio under suspicion. Curiously enough it led to the confession, on Pfeiffer's part, that the Massowah variety with which he had worked for some time, and which had formed the basis of his cholera studies, is an impostor; yet this vibrio had been used in most laboratories, and its specific nature had never been doubted by bacteriologists. On the other hand, a vibrio separated by Ivanoff from a case of typhoid fever was declared to be genuine, although formerly it was excluded from the group of cholera vibrios. Before Pfeiffer's method can be convincing, it must be shown that cholera is specific in the sense that it is caused by one form of vibrio, and only one. If this be so, and if, under such conditions, Pfeiffer was fortunate enough to secure this one vibrio, then the immunity test might become absolute; if the specificity of protective serum within Pfeiffer's narrow limitation can be accepted.

Sanarelli objects that Pfeiffer and Issaeff themselves have shown that normal horse's serum is as active as that of cholera-immune animals; and Roux maintains against Behring's law that antitetanic serum can destroy the lethal effect of snake poisons. Further, Sanarelli's own serum tests led to results very different from those of Pfeiffer; for he obtained reciprocal action between many choleraic and non-choleraic vibrios: he concludes that "it is established that the serum of an animal vaccinated against a pathogenetic organism is endowed with protective action, not only with regard to varieties of the same species, but also with regard to organisms belonging to a different species. The bacteriological diagnosis of the choleraic vibrio by means of anticholera serum, therefore, is a practice not warranted by results."

Dunbar and Klemperer agree with Pfeiffer in regard to the specificity of the cholera serum and its value as a diagnostic test; nevertheless the former acknowledges that a true vibrio may become so altered in its properties that it will eventually react negatively. C. Fränkel and Gruber are neither of them willing to accept the absolute validity of this test. Bordet, however, applying the serum test in a manner differing from that of Pfeiffer, that is, by studying the antimicrobic power of the serum outside the body, to some extent disagrees with Sanarelli, and asserts that this power of a serum is always more marked towards identical vibrios or towards varieties of a species. But yet, we find from his researches that the "Massowah serum" reacts on a Calcutta vibrio, but not on vibrios obtained from Constantinople, Hamburg, East Prussia, and Casino; and that the "East-Prussia serum" reacts also on the

Hamburg and Constantinople varieties, but not on the Massowah vibrio. Bordet believes that the preventive action of the cholera serum is specific to the same extent as its germicidal action. Pfeiffer has asserted that if vibrios inoculated into the peritoneal cavity of a cholera proof guinea-pig become transformed into granular masses, or if the same result follow a similar injection of a mixture of vibrios with specific serum, they are genuine comma bacilli. This granular transformation is called Pfeiffer's phenomenon. Bordet states that the same phenomenon can be obtained outside the animal body on a glass slide, if a little of the suspected culture and normal serum be mixed with a few drops of anticholeraic serum: then if we are dealing with true vibrios they are at once changed into a granular mass. Those vibrios which do not respond to Bordet's reaction fail to respond to Pfeiffer's test; and Bordet therefore proposes his method as a quicker and readier procedure, and also as a less expensive one, since it requires fewer animals. A vibrio which gives a positive reaction may be considered genuine; and Bordet acknowledges that a negative reaction must be accepted with reservation, because some vibrios are more resistant than others. Mr. H. E. Durham, simplifying the test, has recently come to the same conclusion; but he also confesses that the limits of the absolute value of this serum test for the diagnosis of cholera vibrios has yet to be determined, and he adds that a series of gradations in intensity of reaction between serum and vibrios has been observed. It is evident, then, that at present we are surrounded by contradictions, and must suspend our judgment.

Metschnikoff criticised both Gruber's and Pfeiffer's tests adversely; the latter, because it leads us to paradoxical results. Of Gruber's test he says that it is precisely the regularity and circular appearance of young colonies of Deneke's vibrio which have always been taken to distinguish this vibrio from the cholera vibrio: yet in young colonies of Deneke's vibrio we find among the symmetrical colonies others of irregular contour; and among the varieties of cholera vibrio, on the other hand, we find some which present a regular contour. Here then we find no way out of our difficulties. But we may state that the validity of Pfeiffer's tests can hardly be accepted, unless it be shown that morphological and cultural variation is never accompanied by chemical variation.

Metschnikoff is also of the opinion that among the water vibrios found independently of any cholera outbreak there are choleraic vibrios. Of these we shall now speak.

(*c*) Sanarelli discovered a number of vibrios in water, which often could not be immediately traced to any epidemic of cholera, present or past; these he pronounced to be choleraic vibrios, altered or modified by saprophytic conditions of life. We must premise that he accepts the researches of those who maintain that there are varieties of comma bacilli, and who doubt the exclusive specificity of Koch's original organism. This doubt he considers still more justifiable in the light of Rumpel's and Metschnikoff's discoveries of cholera vibrios in the fæces of healthy persons, to which we may add similar observations by Cunningham,

Pasquale, Lesage, and Macaigne. He rejects the criticisms of Hüppe and Friedrich, who attempted to show that all these various forms are merely physiological varieties of one and the same species, and he rejects Koch's six tests also, namely, (1) microscopical examination; (2) cultivation in peptone solution; (3) appearances on a gelatine plate; (4) appearances on an agar-agar plate; (5) the nitros-indol reaction; and (6) the animal test. Sanarelli obtained altogether 32 water vibrios of extreme variability, many of which satisfied even Koch's conditions; and his conclusion was that, in the absence of an epidemic, vibrios may be found which are identical with the true choleraic germs. Now an animal protected against any one of these varieties is not necessarily proof against the others. Sanarelli abandons the narrow conception of morphological and biological uniformity; he believes there are different races of vibrio all capable of causing true cholera; and that we must consider many of the non-pathogenetic forms as varieties which under special conditions may become virulent. Yet since, taken collectively, they resemble one another in many respects, it is very probable that all the varieties obtained from choleraic stools or from water have a common origin, their differences being caused by the saprophytic conditions which they find in water.

In continuing his researches, Sanarelli, after having produced diarrhœa in normal guinea-pigs, separated 12 vibrios from their intestinal tract, which also he regarded as choleraic forms. Pfeiffer's serum test, as already mentioned, he declares, more or less on the same grounds as Metschnikoff, to be utterly inadequate. Sanarelli also disagrees with Pfeiffer in regard to certain varieties which, in his own hands, by means of the serum test, reacted as true choleraic organisms, though Pfeiffer on the strength of the same test had considered them to be non-choleraic; he goes further than this, for he denies, from experiments of his own, the specificity of protective serum, since he succeeded in conferring an immunity on guinea-pigs against choleraic infection by means of anti-typhoid serum, and again by means of a serum obtained from an animal inoculated against the vibrio of Metschnikoff, which is generally acknowledged not to be choleraic. It is not quite easy to follow all Sanarelli's arguments, but it seems that, although he believes in a common origin of all the various choleraic vibrios, he is an opponent of those who insist on a specific comma bacillus; for in his last paper he thus expresses himself: "Nous pouvons conclure qu'il y a des races diverses de vibrions cholériques inégalement virulents."

(*d*) In connection with Sanarelli's work we may consider that of Mr. Hankin, who regards the many varieties of vibrios as degenerate forms of Koch's organism. In his opinion the discoveries of vibrios in the water and elsewhere throw doubt rather on the tests for the cholera microbe described by Koch, than on the authenticity of the cholera microbe as the cause of cholera. He summarises his results, obtained in India, as follows: In a large number of localities, situated often under very different climatic and other conditions, microbes resembling that of cholera are extremely

rare, except in places in which cholera has recently existed. During the epidemic, according to his experiments, they generally show virulence, power of giving the indol reaction, and other characters regarded as typical of the cholera microbe. After the cessation of the epidemic they are greatly diminished in virulence for guinea-pigs; and in their limited ability of growing on agar-agar they betray a diminution of vitality, which he regards as an indication of diminished virulence. Such degenerated vibrios show a great tendency to die out in ordinary cultures, so that it is difficult to keep them alive for any long time. The conclusion he draws is that these vibrios are the cholera microbe in various states of degeneration. The cessation of an epidemic is due to a weakening of the microbe. Whether the degenerate microbes can under any conditions regain their virulence, and thus again become capable of starting an epidemic, is a question he leaves unanswered. Such a view is simple, but it is too simple; and Hankin evidently relies on a guinea-pig test, which all other workers consider unsatisfactory. We cannot allow that all the varieties described by Cunningham and others can on such evidence be neglected as degenerate forms of one and the same microbe.

It is manifest that at present the argument is extremely involved, and that it is impossible to come to a definite decision. It appears that most observers who have studied the question associate comma bacilli closely with cholera: some of these uphold the unity of the vibrio, others accepting this unity declare that its forms are manifold; and forms which some regard as varieties of one species of organism, others describe as distinct species. Rumpf sums up his experiences gathered during the Hamburg epidemic in the former sense, and concludes that undoubtedly Koch's comma bacillus is the cause of Asiatic cholera, and that its home is the Ganges. Human intercourse diffuses it, but a phase outside the human body, that is, an ectanthropic period of existence and development there must be. This phase is frequently passed in the water where the comma bacilli experience changes in infective virulence. Long seasons of warmth favour their development, rains and cold inhibit it; but beyond India they cannot gain a permanent footing, although they may survive for months and years under suitable surroundings, gradually losing their original features; these, however, they may regain under given conditions and for a given time. Carried away by the rivers and streams, they reach the digestive tract through the water, in some cases perishing at once, in others passing away harmlessly, and in yet others producing lesions varying in intensity from diarrhœa to typical cholera. Personal disposition in this connection is of far reaching importance. These views are evidently a modification of those originally held by the contagionist school, but years must elapse before a complete solution of the problem is found.

A few matters still remain to be discussed in the light of recent knowledge: these are (1) the pathogenetic properties of the comma bacilli; (2) their chemistry; (3) the production of immunity in animals and in man; and (4) the vitality of the vibrios outside the human body.

1. The Pathogenetic Properties of the Comma Bacilli. — (*a*) We have

already referred to earlier animal experiments on the pathogenetic properties of the cholera vibrios. These, however, were hardly convincing, and, a few exceptions apart, it has generally been admitted that it is impossible to produce a true choleraic state in animals. Recent researches have shown that intraperitoneal inoculation of guinea-pigs is generally followed by death; and this reaction at one time was thought by Koch and Pfeiffer to be characteristic of the true vibrios: we now know, however, that no reliance can be placed on this test. It was further thought that the results following such intraperitoneal inoculation are specific, and therefore of great value for the purpose of diagnosis. But Klein has conclusively demonstrated that the same symptoms and the same anatomical changes follow intraperitoneal injections of other bacterial forms, such as the vibrio of Finkler-Prior, the bacterium coli, the bacillus prodigiosus, proteus, and others; and his observations have been confirmed by Sobernheim, Gruber, and others. Hence there is nothing specific in this animal reaction. Sanarelli likewise maintains that the enteritis which may be produced by infection with choleraic vibrios is not specific, and is identical with that produced by other organisms or their toxins. According to Gamaleia, on inoculation a disease not unlike cholera appears in dogs, with the symptoms of vomiting, diarrhœa, convulsions, cold and cyanosis.

In considering the immunity of man under certain conditions of season and locality, the two factors especially dwelt upon by Pettenkofer, the question arose in the mind of Metschnikoff whether the presence of other micro-organisms in the intestinal tract may co-operate in this result. Kitasato had worked at this problem in 1889: using artificial media, he found that the growth of cholera vibrios was generally not arrested by the presence of other micro-organisms — on the contrary, that cholera vibrios checked and even destroyed a variety of bacilli in a few days. Kitasato, however, found some exceptions to this general statement; the bacillus pyocyaneus, for instance, is stronger than the cholera vibrio. Metschnikoff was able to confirm this latter statement, and found, by culture on artificial media, that cholera vibrios are extremely sensitive to the presence of other organisms, and when subject to these conditions undergo certain developmental and morphological changes. He then proceeded to inquire whether the immunity of animals against intestinal cholera could be explained by postulating some action of intestinal micro-organisms antagonistic to the cholera vibrios.

For this purpose Metschnikoff used suckling rabbits, in whose intestinal canal micro-organisms are scanty and of few kinds. By experiments on artificial media he found that certain species of torula and sarcina were favourable to the development of cholera vibrios. On infection by the mouth with the Massowah vibrio, together with a torula and a sarcina, four rabbits, aged 4 to 8 days old, were attacked with fatal cholera; but death did not occur for 7 to 9 days. In a second series of experiments he used a combination of cholera vibrios, as arcina, a torula, and a bacillus (related to B. coli); of twenty-eight rabbits two only sur-

vived, and death frequently occurred in 36 to 48 hours. On section the small intestine, especially the ileum, was hyperæmic, and the cæcum was distended with a fluid which often recalled the characteristic appearance of the watery stools in man. Microscopically the small intestine more especially contained the cholera vibrios; in the majority of cases in pure culture. The cæcum, while also presenting numerous vibrios, always contained other bacilli besides. By examining animals at various stages of the process it was found that the torula, sarcina, and colon bacillus, originally added, disappeared in a few hours; so that the result was not a mixed infection, but possibly one similar to that seen in inoculations with the tetanus bacillus which requires the association of other organisms or of its own toxin to produce the fatal spasms. Nor can the process be regarded as a simple intoxication; for Metschnikoff describes thirteen cases of spontaneous infection among broods of rabbits suckled by the same mother. Here the quantity of infective material had been small, too small to account for the fatal result on the hypothesis of intoxication. These results were only obtained with suckling rabbits; when the young had fed on green food they were no longer susceptible.

Of young guinea-pigs similarly treated thirteen out of seventeen died; but diarrhœa was a rare occurrence, and the post-mortem appearances were far less pronounced. On the other hand the vibrios were found in the blood of the heart in thirteen cases.

Dunbar maintains that the specificity of Koch's cholera vibrio has actually been proved by the experiments of Sabolotny who, like Metschnikoff, asserts that he has produced true cholera in animals. He fed Marmots (*Spermophilus guttatus*) with common bacilli, and thereby produced an infection presenting the classical symptoms of Asiatic cholera; of this malady 50 per cent of the animals died. They became prostrate, refused food, their temperature fell from 38° C. to 32° C., clonic spasms and cyanosis appeared, and after death the gut was filled with fluid, often sanguineous, and containing white flocculi, which consisted to a great extent of cholera vibrios. However interesting these observations of Metschnikoff and Sabolotny may be, they carry less conviction on account of the very special nature of the animals used. It is practically useless to look to inoculations of rodents or dogs or of any animal for positive proof. Inoculations of pigeons by some observers are stated to be a distinguishing test between true and spurious cholera vibrios, the former having no effect on these animals. Sawtschenko and Weichselbaum, however, showed that though generally immune, pigeons succumb occasionally; and Salus found that they can frequently be infected with the true cholera vibrio as readily as with Metschnikoff's vibrio: herein he is confirmed by Rumpel, Weibel, and others, so that this test also, once vaunted, had to be abandoned.

(*b*) Experiments on man have contributed much towards establishing the infective nature of the cholera vibrios. Pettenkofer, Emmerich, Metschnikoff, and Hasterlik collectively report observations made on eighteen persons, who swallowed pure cultures of vibrios. In some cases

severe symptoms followed, in others none, in others again slight diarrhœa. The cases described by Macnamara, who saw five persons out of nineteen fall victims to cholera after drinking water which had been contaminated with choleraic dejecta; the well-known case of Örgel of Hamburg; Koch's equally famous case; as well as that of Freymuth and Lickfelt, where cholera had been acquired in the laboratory; or the experiments of Bochefontaine and Klein, cannot be used as arguments for or against the question under discussion: there is no evidence that pure cultures had been used in these cases. We may ask, indeed, whether the other cases are convincing? The doubtful critic may maintain with some justice that they are not, for amongst the eighteen persons not one succumbed to the infection. Yet Metschnikoff, whose opinion is of great value, declares that in at least one case he observed the symptoms of true cholera to follow the drinking of a pure culture of Koch's vibrio; and that, in spite of the variability of the comma bacillus, there is no reason to doubt that it is the specific cause of cholera. We must refrain from expressing a positive opinion, for evidence based on young sucklings and marmots, and on a few cases of diarrhœa is insufficient, although it brings us nearer to a solution of this vexed question. Pettenkofer, indeed, who for more than ten years was an avowed opponent of Koch's views, has been constrained, on the strength of the observations of the last three years, to acknowledge the vibrio as the specific organism of cholera.

We must also point out that Haffkine's patient anticholeraic vaccinations in India have contributed much to establish this hypothesis. Haffkine is firmly convinced that the cause of cholera is one variable vibrio; and for the purpose of vaccination he uses living cultures of that which he considered to be the choleraic vibrio. He originally prepared two vaccines, a weakened first virus and a strengthened second virus; so that the principle of his inoculations is the same as that practised in the case of anthrax. Now if his operations have been accompanied by adequate success, it may be argued that they will go far to establish the specific action of the cholera vibrio, and also to prove that we are dealing with one organism of protean shapes. His results up to this date have been very satisfactory. Thus in Calcutta he found that the mortality among the inoculated was 17·24 times less, and the incidence of cholera 19·27 times less than among the non-inoculated; so that the present evidence is certainly in favour of the anticholeraic vaccination. If further observations confirm the results already obtained, we can hardly any longer doubt the specificity of the cholera vibrio. The test of experience on man is therefore that best calculated to carry conviction.

2. Chemistry of the Cholera Vibrio. — A few words on the nature of the cholera toxin will suffice, since our knowledge of it is still very imperfect. Scholl obtained from cultures in eggs a toxic peptone which, however, according to Gruber and Wiener, can be obtained from uninfected eggs. Emmerich and Tsuboi explained cholera as a nitrate intoxication, but their fallacies were disproved by Klemperer, who showed that cholera vibrios which have lost the power of forming nitrites remain

virulent nevertheless. Pfeiffer assumed that the poison is protoplasmic, and contained in the bacterial cells; others assumed that this poison is not specific, but is a substance common to many bacteria (a protein, Klein's intracellular poison). Brieger, it may be remarked, had formerly separated six ptomaines from impure cholera cultures; and Gamaleia had anticipated Pfeiffer when he described two poisons belonging to the group of nucleins and nucleo-albumins which he had extracted from the bodies of the vibrios: while Wesbrook showed that the nature of the cholera products varies with the medium in which the vibrios grow. Passing over the numerous observations made by various writers, it may suffice to say that none of the substances separated so far, whatever their nature may be, is capable of producing in animals the symptoms characteristic of the disease in man; the chemical identity of the products formed in the body of choleraic individuals and of those developed in artificial media has not yet been proved. It must be remarked, however, that with most of the substances mentioned, different as their nature may be, an artificial immunity may be produced in the animal.

3. On Artificial Immunity little need be said since, as we have seen, animal experiments have not as yet been of much assistance; indeed, they have contributed rather to our confusion. Haffkine, as already mentioned, employed Pasteur's method of vaccination with attenuated and strengthened living virus. Immunity by means of living cultures may be produced by subcutaneous or intraperitoneal injections, but also by means of the introduction of vibrios through the mouth; indeed, some observers maintain that the highest degrees of immunity are obtained by feeding. With regard to the methods of protection there exist two views of the pathogenesis of cholera. Some consider the lesions naturally occurring in man, and artificially produced in animals, to be due to intoxication; so that in order to produce an immunity all that is required is to render the body toxin proof: the seat of infection is of secondary importance. Others believe that the locality where the vibrio thrives cannot be neglected; and that an immunity of the skin or peritoneum, for example, does not imply an immunity of the intestinal tract. The latter experimenters assert that guinea-pigs, immune on subcutaneous or intra-abdominal inoculation, are still susceptible to an infection by the mouth. There is, however, considerable diversity of opinion on this point. Metschnikoff, experimenting on man, was inclined to believe that the intestinal tract cannot be rendered cholera proof by any form of artificial infection; while Sanarelli, maintaining that cholera is a toxic enteritis, contends that a cholera immunity must depend on an acquired tolerance of the cholera poison by the intestinal walls. Sabolotny agrees with Metschnikoff that subcutaneous or intraperitoneal treatment does not, in the case of marmots at least, protect against gastric infection.

It is important to know whether one form of choleraic vibrio protects against all others. According to Pfeiffer, the action of all true comma bacilli is reciprocal, but there is no reciprocity in protection between the true and false vibrios. An immunity established by intraperitoneal in-

jection of one organism may lead to a merely transitory immunity from another and different organism, but to a lasting immunity from identical organisms. An animal protected against the cholera vibrio is still susceptible to the vibrio of Metschnikoff. This is the fundamental principle of his serum test. On the other hand, Sabolotny asserts that artificial immunity procured with one variety does not necessarily imply protection against others; and many observers — such as Salus, Weibel, and Sanarelli — maintain that there is a reciprocal protective action between the vibrios of Metschnikoff and the true cholera vibrios. This seems to be so well established, that, if we accept the theory of the unity of the vibrios, we are almost forced to find a place for this organism in the long series of choleraic forms; an admission hardly calculated to make matters easier, but nevertheless the logical outcome of laboratory observations. Haffkine's experiment in India seems to show that by means of one variety of the comma bacillus an immunity can be produced in man against all other true vibrios. Thus once more we come face to face with contradictions which may find their natural explanation in the variable conditions of experiment.

Numerous experiments have also been made with serum, and the fact is established that an animal may be protected against a cholera peritonitis by means of a specific serum. Klemperer and others showed that the serum obtained from individuals who have recovered from cholera has a marked protective action, and that the serum of artificially protected animals is equally potent. These observations ought to be regarded as an additional proof of the specificity of the comma bacillus; but Metschnikoff and others have shown that normal serum is frequently thus active, and we have said that horse's serum, according to Pfeiffer and Issaeff, possesses similar protective power. Nevertheless it is generally accepted that to confer an immunity from cholera upon an animal is to render its serum anticholeraic; and experiments have further shown that by gastric inoculations also this result can be obtained. We have referred above to the conflict of opinion on the specificity of the serum of protected animals, and we do not wish to reopen the matter. Whether a therapeutic serum will ever be found for cholera must be left to the future; suffice it to state here that Behring is firmly convinced of its possibility, and is at the present time striving hard to secure it. The various views held from time to time with regard to a natural cholera immunity need not detain us further than just to allude to the ingenious explanation put forward by G. Klemperer, who believes that it depends on the nuclein substances of the intestinal epithelium which possess marked antimicrobic power.

4. Vitality of the Cholera Vibrio. — If we assume that the vibrios are the cause of cholera, we are forced to meet the objections of those who deny their ætiological importance on the ground of their want of resistance to external influences. If we are to accept the opinion mentioned above, that the various water vibrios are but degenerated or altered forms of one species, we shall find less difficulty in explaining outbreaks

or sporadic cases of cholera. But, apart from this unproved hypothesis, recent observations have shown that the choleraic vibrios are more resistant than is generally supposed. (*a*) These organisms may find an abode in persons actually or apparently healthy. Thus during the winter epidemic of 1892–1893 the presence of Koch's vibrio was demonstrated in the Hamburg Hygienic Institute, in twenty-eight healthy persons; and also in the members of certain families similar observations were made. These twenty-eight persons had been in contact with cholera patients, and their stools were solid or semi-solid. Abel and Claussen found vibrios in the fæces of 13 out of 17 healthy persons who had been in daily intercourse with cholera patients. (*b*) In the stools of convalescents from cholera vibrios were found after 50, 47, 27, 16, 10, and 8 days; and (*c*) it has been shown that they may remain alive and capable of proliferation in choleraic dejecta for a considerable time. Thus Gruber isolated vibrios from a stool which had been kept for 15 days; Karlinski from stools 52, 37, and 28 days old; while Dunbar succeeded in the same search after 76, 143, and 163 days, and occasionally even after 8 months. (*d*) As regards artificial cultivation, the cholera vibrio has been shown to be highly saprophytic. Thus, according to Fränkel, it thrives in solutions of 0·4 per cent aspartate of sodium, and in water it will also remain alive for some time; on potato boiled in salt solution it grows well at the ordinary temperature, and even at 8° C. In ordinary milk it survives 12 hours to 6 days; on fruit and fish for some days. (*e*) From flies fed on choleraic material the vibrios could be separated after 14 days; on silk threads they remained in a vital condition for 13 to 86 days, and dried on glass for 120 days. (*f*) Even severe degrees of cold can be resisted for a few days; the concurrence of saprophytes, according to Kitasato, has but little influence on them; but acids soon destroy them. (*g*) In water they remain alive for many days; in sterile distilled water for 73 days to a year; in sterile well-water for months, but in unsterilised water for from 4 to 25 days. Örgel, indeed, succeeded in keeping them alive in ordinary Elbe water for almost a year. Hence these vibrios are possessed of no little tenacity; and, if they be the cause of cholera, there is no difficulty in explaining the spread of an epidemic, so that Pettenkofer's early objection — already withdrawn by himself — falls to the ground.

Summary. — If we now review shortly our position with regard to the bacterial ætiology of cholera, we find that (1) vibrios are so constantly associated with the disease that their absence may justly be taken as an error in observation; (2) vibrios are frequently found in pure culture to the exclusion of other organisms. (3) These vibrios are possessed of great variability, both morphologically and biologically; so that new forms, widely different from the original stock, can readily be produced in the laboratory. We have, therefore, some justification in regarding the various kinds of vibrios obtained from cholera dejecta as descendants of one species; but we have as yet no means of proving this assumption. (4) None of the various tests, taken singly, suffice to

establish the unity or specificity of the vibrios; but the circumstantial evidence is fairly strong — indeed, so far as our present knowledge goes, almost convincing. (α) Pfeiffer's test, with its modifications, although not an absolute one, has proved the true nature of a very large number of vibrios obtained from undoubted cholera cases, or from sources where contamination had taken place; though in some instances it has broken down. (β) Further, there is the evidence of Klemperer that the serum of persons who have recovered from cholera has protective powers against inoculations of animals with cholera vibrios; and that, conversely, the serum of animals rendered immune by means of choleraic vaccination displays the same powers. True, normal serum often has the same action, but certainly to a less degree. (γ) Within certain limits this action of the serum of protected animals is specific. (δ) Lastly, there are the observations of Haffkine in India, who finds that the subcutaneous inoculation of a true vibrio will protect man against Asiatic cholera. The various lines of argument all then converge towards one point, namely, the unity and specificity of the choleraic vibrios. Time will show how far this classification is final.

We shall conclude this account with directions to guide the physician in the bacteriological diagnosis of cholera; but we must premise that, comparatively simple as this is in skilled hands, it cannot be undertaken by persons unfamiliar with bacteriological methods.

Bacterial Investigation of Bowel Contents and of Dejecta. — The methods here summarised were those used by Dr. Klein in his examination of reputed cholera material during the occurrence of cholera in England in 1893. The cases may be classified broadly in two kinds: (1) *Those in which microscopical examination showed crowds of comma bacilli in the mucous flakes;* and (2) *Those in which at the outset comma bacilli, as compared with other bacilli, were in a small minority.* It is in cases of the latter kind, which present the greater difficulty, that the value of Method 3 is recognised. On the other hand, when the comma bacilli are originally present almost in pure culture, other methods are equally good.

Method 1. — A flake from the dejecta is placed in peptone broth, and incubated at 37° C. In 24 hours an abundant crop of vibrios is found in the superficial layers of the broth. This pellicle consists of a practically pure culture, or at any rate is a culture which easily allows of pure subcultures being obtained.

Method 2. — A flake is placed in sterile salt solution or broth; it is shaken up, and from this gelatine or agar tubes are inoculated, and plates are made. In agar plates incubated at 37° C., numerous colonies may be found in 20 to 30 hours. In the gelatine plates, after 2 to 3 days' incubation at 20° to 22° C., numerous typical colonies can be got.

Method 3. — A flake is placed directly into Dunham's peptone salt solution (1 per cent peptone, 0·5 per cent sodium chloride), or the Dunham's solution is inoculated after previous dilution of the material. The peptone solution, after 6, 8, to 10 hours' incubation at 37° C., shows a definite turbidity, due to the rapid growth of the comma bacilli; and the cholera-red

reaction may be obtained. For speedy diagnosis this method is most valuable: in 6 to 12 hours, or at latest in 16 hours, comma bacilli can be found in the superficial layers of the peptone solution, so that in 24 hours pure sub-cultures and the cholera-red reaction can be obtained in secondary peptone tubes. Also a positive result may be got by this method in cases in which the microscopical examination has failed to give definite evidence of the presence of vibrios.

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Clinical, Pathological, and Therapeutical Aspects of Asiatic Cholera

Symptoms of Cholera. — In different epidemics and different individual cases these present considerable variation. It will be most convenient to describe, in the first place, the phenomena of an ordinary seizure — the form of disease most frequently met with; and then briefly to delineate those less common manifestations which are seen during the course of epidemic outbreaks, and seem to owe their exceptional character to variations in the strength and amount of the poison, or to peculiarities in the constitution and proclivities of individuals who have been subjected to its influence.

The Ordinary Form. — In a characteristic case of cholera it is always possible to distinguish certain well-marked stages which have been designated by their most striking features. A premonitory or incubative stage can be recognised in a large proportion of cases, followed by the stage of evacuation, of which purging, vomiting and muscular cramps are the most prominent phenomena; to this succeeds a stage of collapse, characterised, as the name implies, by profound depression of all the functions of the body; finally, a stage of reaction, in which more or less febrile excitement is manifested, ends, in favourable cases, in recovery.

The *stage of incubation* is that which intervenes between the reception of the poison and the manifestation of serious and characteristic disturbance of health. Its duration varies from a few hours to a few days, probably not exceeding ten. Three to six days appear, inferentially, to be the usual length of this stage; though precise and positive knowledge is wanting, owing to the lack of exact information as to what enters the body and how and when it effects an entrance. The symptoms of deranged health which may be felt or observed during this period are referable to gastro-intestinal irritation, and to a disturbed or depressed condition of the nervous system. Diarrhœa is the most common precursor of cholera: it may last for hours or even days, and is apt to be copious and watery, motions being passed three or four times a day; it may be painless or accompanied with griping. There is often a feeling of weight or oppression at the pit of the stomach, and there is reason to believe that in this stage the function of digestion is seriously impaired (Chevers). The nervous symptoms take the form of malaise, depression

of spirits, pallor, anxious expression, exhaustion, giddiness, tinnitus and headache.

In most cases premonitory symptoms are not noticeable or are very transient; and the disease sets in without warning, with violent purging and vomiting, speedily followed by cramps and progressive exhaustion. These are the essential phenomena of the *stage of evacuation*, which may last from two to twelve hours or longer — the duration depending probably on dosage and vital resistance. The purging is frequent, copious and watery. The earlier stools are fæculent, the later pale, resembling whey or water in which rice has been boiled — a flocculent or curdy sediment being deposited on standing. Later motions are sometimes sanious. Successive evacuations should be received in separate vessels for observation and comparison. There may be griping or abdominal pain; more frequently there is neither. The bulk of material passed in this stage is often very large. Vomiting generally begins later than purging: the contents of the stomach are first expelled; and it has been observed that these are often undigested, though they have been in the stomach for some time. The later rejections are watery and copious, emitted with force, and occasionally tinged with blood. Vomiting is easily excited by ingesta, and these are generally returned sooner or later. In some cases distressing and exhausting retching occurs without much result. The reaction of the vomited material varies; it is sometimes very acid. Muscular cramps are a painful feature of this stage; they may begin with the purging, and be prolonged into the next stage. The legs are their most frequent seat; but the muscles of the abdomen and back, and in some cases the whole muscular system may be affected; the cramped muscles feel hard and knotty, and in many cases the pain is very severe. The temperature of the body falls somewhat as this stage proceeds, the surface becoming cold, dusky, clammy, or covered with sweat. The features are drawn, eyes sunk, expression anxious or blank, fingers and toes shrivelled, tongue white and cold. There is great thirst and much restlessness. The breathing is not thus far much affected, but the pulse rises in rate and loses in force. The patient becomes greatly exhausted, and, though generally sensible, is apathetic. Recovery may take place in this stage by cessation of purging, vomiting and cramps, and gradual restoration of strength; but in the majority of cases a more profound depression of vitality sooner or later supervenes. This is the *stage of collapse*, into which the patient may lapse gradually or suddenly. It may last from two or three to forty-eight hours, or even more, the attention being withdrawn from the evacuations, and arrested by the signs of alarming exhaustion. Liquid, colourless motions may still be occasionally passed involuntarily; or the presence of watery material may be detected in the intestines by palpation or succussion. Vomiting or attempts to vomit may persist, and cramps are often present, sometimes terribly painful. But these symptoms are overshadowed by the evidences of failing power: the pulse flickers and fails at the wrist, and is sometimes imperceptible in the brachial and almost so in the femoral arteries; its rate, always

accelerated, may rise to 120 or 140, or even higher. The heart sounds get less distinct, especially the first: in some cases strange murmurs and friction sounds are detected in this stage (Wall), which betoken disturbed and inco-ordinate contraction of its walls or the existence of clots in its cavities.

The capillary circulation becomes slow and feeble, the surface gets livid; respiration is quick and shallow, painful and often paroxysmal dyspnœa arises, compelling the sufferer to struggle for breath; the expired air is cold and deficient in carbonic acid. The face presents the characteristic choleraic expression — features pinched, skin drawn, eyeballs sunken and surrounded by a dark areola, lids half closed, pupils contracted, mouth open, teeth covered with sordes, tongue cold, countenance apathetic. The general surface is cyanotic and clammy or bedewed with cold sweat: the fingers and toes are wrinkled. There is great restlessness and profound debility. The intelligence is clouded, the senses impaired, the muscular power diminished: in some cases sense and sensibility and capacity of movement are retained; in others coma or a semi-comatose state exists. The voice is husky and feeble, or the patient can speak only in faint whispers. Thirst is imperative, and a feeling of coldness is felt. The urine is suppressed; the bladder is generally emptied in the preceding stage, and no further accumulation of urine takes place. The temperature of the surface and mouth is greatly and, in fatal cases, increasingly depressed, and may fall below 90° F.; the temperature of the axilla is higher, but yet below normal, readings of 95° to 97° F. being not uncommon in this stage; the rectal temperature may be slightly subnormal or normal, but in time it shows a tendency to rise above the normal.

In this stage a peculiar and characteristic odour may be detected in the breath and from the skin. The motions are devoid of smell unless they are retained, in which case they quickly become offensive. It is in this stage of cholera that death most frequently occurs; and the fatal event may happen early or late, very suddenly or after some lingering hours while life and function are slowly waning. Death may occur by apnœa, asthenia or coma.

The *stage of reaction* is, generally speaking, characterised by a gradual restoration of power and resumption of function. The pulse returns to the wrist, feebly and fitfully at first; but there is, in favourable cases, a progression in steadiness and strength. The breathing becomes easy and the patient tranquil. Blueness, coldness, shrinking and clamminess of the skin give way to roundness and warmth. Temperature is normal or slightly raised. The stomach regains its tone, and food is retained. The stools resume their proper colour; some looseness may persist, but the motions are less frequent and less watery, and exhibit successively deepening tints of gray and brown. Urine is passed, though its reappearance may be delayed for many hours; it is at first scanty, high coloured, of strong smell and high specific gravity, albuminous, and containing indoxyl and casts; then it becomes watery and

copious. Mental activity and muscular power return, and complete recovery may take place within a few days.

So happy a result is, however, by no means invariable. In a considerable proportion of cases (from 10 to 25 per cent) events occur during the stage of reaction which constitute a serious departure from the normal sequence, and prolong the illness or cause death.

The variations which take place in the symptoms and course of cholera are numerous and well marked, and have led to **the distinction of several forms of the disease.** These varieties of cholera are apt to present themselves more or less prominently in different epidemics and at different periods of the same epidemic; and, for purposes of diagnosis and treatment, it is highly important to take them into account. They are best described in the order of succession of the phases of the ordinary disease.

1. The disturbance of health may be slight and transient. During an epidemic of cholera many persons complain of slight malaise, anorexia and looseness of bowels which pass off with or without treatment. This is the so-called *ambulatory* form. The disease appears to be arrested or abortive in the incubative stage.

2. In other and more frequent cases the diarrhœa is more pronounced and persistent — painless, accompanied, perhaps, with nausea or vomiting, and sometimes with cramps. The stools are copious and watery, inclining gradually to the rice water type. There is no suppression of urine. Cases of this kind occur in anticipation of or during an epidemic, and contribute to that excessive prevalence of diarrhœa which statistics indicate as generally concomitant with cholera. With or without the aid of medicine recovery usually takes place within twenty-four hours; but not unfrequently such cases, especially if untreated, lapse into true cholera. This form of disease has received the name of *choleraic diarrhœa* or *cholerine*, and appears to represent an arrest in the stage of evacuation.

3. On the other hand, this stage may seem to be absent, patients passing quietly into fatal collapse without either vomiting or purging. Cases of this sort have been described as occurring at Karachi in the year 1846, and at Teheran in the same year. On post-mortem examination, however, the characteristic lesions and evacuations of cholera are found in such cases. The absence of evacuation and the rapid prostration have been attributed to the large dose or special virulence of the poison which rapidly overpowers vital resistance and energy. This form of disease is very rare; it has been called *cholera sicca*.

4. The stage of collapse is very short; death takes place suddenly from apnœa, with symptoms of gravely disturbed cardiac action and impeded circulation through the lungs. This may depend on spasm of the pulmonary arterioles, on the difficulty of transmission of the inspissated blood from the right heart into the lungs, or on the formation of clots in the right cavities. Dr. Wall has described murmurs and friction sounds which he attributes to this cause: the condition is not necessarily, though frequently fatal. It may be called the *embolic* form or phase of cholera.

5. On the other hand the cold stage may be prolonged up to thirty-six or forty-eight hours. Recovery sometimes takes place in such cases, but the unfavourable contingencies of the reaction stage are more likely to occur under these circumstances.

6. The intelligence of the patient — in other words, the activity of the brain and nervous system — is in some cases marvellously keen during the stages of evacuation and collapse; but a condition of growing prostration and apathy is the rule. In some instances the clouding of the intellect and dulling of the senses are early and profound, and out of harmony with the other symptoms. This *primary choleraic stupor* has been attributed to the direct effects of the choleraic poison on the nerve tissue (Wall).

The varieties of cholera depending upon variations in the phenomena and course of events in the stage of reaction are numerous and important.

7. The *reaction may be imperfect.* Some revival from collapse may occur, but the temperature remains subnormal, purging and vomiting continue, the pulse does not regain power, exhaustion is progressive, and the patient in time sinks from asthenia, or may pass into a fatal typhoid phase.

8. In other cases, after temporary amelioration, there is a *relapse* of the purging or vomiting, and death by exhaustion sooner or later ensues, though recovery from the relapse is possible. The relapse may be induced by the use of purgatives or indiscretion in diet.

9. A very serious variety of cholera is the *hyperthermic form*, in which during collapse the rectal temperature is found rising to 100° F. and over. The axillary temperature soon follows suit, and a very high degree of heat (as much as 107° F. in the axilla, and 109° F. in the rectum — Wall) may be reached. Such cases are very fatal.

10. During the stage of reaction patients not unfrequently lapse into a *typhoid state.* This does not depend on excessive temperature or on suppression of urine, but seems to correspond rather with the state of "prostration with excitement" met with under other circumstances. The symptoms are those of the typhoid condition however caused — moderate elevation of temperature (101° to 102° F.), excitement of pulse and respiration, failing power, restlessness, delirium, subsultus, dry tongue and lips, sordes, stupor merging into coma, and in prolonged cases purpura and bed-sores. This condition is generally, but not necessarily fatal. Convalescence is very slow in the non-fatal cases. There are cases which seem to occupy an intermediate position between the hyperthermic and the typhoid cases; in these mild fever of an intermittent or remittent form complicates and delays recovery.

11. In these febrile states *eruptions* sometimes make their appearance. The more common are urticaria and erythema: the latter may be bright in colour and widely diffused. Roseola, maculæ and bullæ have been described. The eruption in such cases may perhaps be considered a sort of exanthem.

12. Suppression of urine, and the consequent *uræmia*, constitute the

most important and anxious feature of an abnormal reaction. The re-appearance of urine is sometimes delayed for many hours or even days without serious results; but such delay is always a cause of anxiety, and in most cases of prolonged suppression cerebral symptoms attest the retention of waste matters in the blood. Stupor with restlessness, muttering delirium, spasmodic contraction of muscles, bloodshot eyes, contracted pupils, dry lips and tongue, sordes, vomiting, slow pulse are the chief symptoms; the patient often relapsing into fatal coma. The bowels may remain relaxed; this is favourable and should not be checked. Vomiting of grass green material has been noted in this state. The secretion or discharge of bile may be suspended, and this adds to the gravity of the case. Chevers has described this dual suppression as cholouræmia. On the re-establishment of the urinary secretion the alarming symptoms may subside and convalescence proceed.

The Sequelæ of Cholera. — A number of untoward events may arise during the stage of convalescence; they may be classified as follows: —

1. *Functional.* — Under this head are included anæmia, debility, nervous depression, jaundice (a rare but dangerous complication), gastric irritability, persistent hiccough, insomnia, dementia, paraplegia, anasarca, irregularity of bowels and chronic diarrhœa. In pregnant women abortion is almost invariable; the child dies during the algide stage and is sooner or later expelled. Signs of cholera are often found in the fœtus (Wall).

2. *Inflammatory.* — Œdema of the lungs, bronchitis, pneumonia and pleurisy are not unfrequently met with, especially in conjunction with suppression of urine. Meningitis, conjunctivitis, arthritis and parotitis have also been described. The parotid inflammation sometimes ends in abscess. Dysentery is an occasional complication of convalescence, but it is mild in type and amenable to treatment.

3. *Destructive.* — Ulceration of the cornea is not uncommon. Bedsores sometimes form in low cases of typhoid character and uræmia if the nursing be defective. Gangrene of the nose, ears, penis and scrotum, more rarely of the fingers and toes, are also met with, especially among natives of India. The dead parts, if limited, may be separated and cast off, but extensive gangrene is generally fatal.

Pathology and Pathological Anatomy. — The morbid changes disclosed by post-mortem inspection of cholera cases vary with the stage of the disease in which death took place. As a general rule alterations in blood distribution are the most prominent feature of early deaths. Epithelial disorders of mucous tracts and evidences of glandular irritation occur later; and in more protracted cases, indications of more serious structural changes — inflammatory or necrotic — may be seen. The **morbid anatomy** of typical cholera is characteristic and constant. The surface of the body retains the peculiarities already described, which need not be repeated. Post-mortem rigidity appears early and lasts long. In some cases muscular contractions occur soon after death and cause distortions of the body.

The *digestive tract* reveals signs of grave disorder which are usually most marked towards the termination of the ileum. The stomach is generally empty; its lining membrane is usually congested, the degree of hyperæmia varying; ecchymoses are occasionally seen and, rarely, hæmorrhage into the cavity; a state of catarrhal inflammation is sometimes found; the contents may be acid, neutral, or alkaline; the duodenum and jejunum usually exhibit hyperæmia, either continuous or patchy, arborescent or capillary. The lining membrane is generally swollen and sodden, and a pulpy material can be scraped off it, which consists mostly of granular cells and amorphous protoplasmic masses. Enlargement of Brunner's glands has been described (Griesinger), and denudation, often extensive, is frequently seen. Whether this shedding of epithelium be the result of a necrotic process during life or a post-mortem detachment is a subject of doubt and dispute.

The ileum participates in the changes occurring higher up, but the last twelve or eighteen inches of it exhibit them more strongly and sometimes this portion shows special signs of diseased action. The solitary glands are enlarged and stand out prominently, and Peyer's patches are congested and swollen. This portion of the gut may also be covered with a croupous or diphtheritic pellicle, more or less adherent to the surface, and flocculent processes may project into the lumen of the tube, and may occasionally fill and obstruct it. Separation of this material may give rise to excoriation or even to ulceration. Ecchymoses of the walls and hæmorrhages into the cavity of the small intestine sometimes occur.

The large intestine is generally less seriously diseased than the small. Congestion and catarrhal inflammation may occur, and in rare cases ulceration giving rise to hæmorrhage.

The walls of the intestinal tube are generally thickened, and the lumen contracted. The peritoneal surface is injected, and presents, as Dr. Wilks has observed, a characteristic rosy colour. The peritoneal cavity contains no fluid. The mesenteric glands are enlarged, hyperæmic, and infiltrated with a whitish granular exudation (Aitken).

The **contents of the intestines** vary in quantity according to the amount of vomiting and purging during life; they vary in quality according to the stage of the disease and intensity of the morbid process.

The cholera stool is a turbid, gray or grayish white liquid, resembling water in which rice has been boiled. On standing, a granular, curdy or flaky material subsides, leaving a whey-like supernatant fluid. The reaction of the material is alkaline, and its specific gravity from 1005 to 1015. The material found in the intestines after death resembles the sediment which settles from the evacuations passed during life. The solid elements in a motion amount to from 10 to 30 parts per 1000, the soluble salts from 5 to 10, and albumin and extractives from 2 to 20 (Parkes). The amount of albumin is small, but of salts — sodium and potassium chloride, sodium phosphate, carbonate and sulphate — considerable. Nitric acid sometimes gives a red reaction. Considered as a

derivative from the blood the cholera evacuation accounts for a large loss of water, a large loss of soluble salts, and a moderate loss of albumin and animal matter.

The *microscopy of the intestinal discharges and contents* has been the subject of laborious investigations. The objects found are embraced in the following categories: —

1. Débris of food.

2. Results of epithelial proliferation and glandular irritation — amorphous, granular, and protoplastic masses, granular cell forms, and cloudy epithelia. The amount of epithelial cells found in the contents after death exceeds that discovered in the stools during life.

3. Red blood cells and leucocytes. Much of the protoplasmic granular material which forms so large a proportion of the solid constituent of the stool is held to be derived from changes which have taken place in white cells that have migrated from the blood (Lewis).

4. Organisms; some peculiar to cholera, others incidental to it. The bacteriology of the disease has been already described.

The *liver* is generally affected with venous congestion, the colour being dark, and venous blood escaping on section. The gall bladder is full of bile, which in later stages is thin and watery. Shedding of the epithelium of the bile ducts has been described. There is no mechanical impediment to the discharge of bile through the ducts.

The *spleen* is not enlarged; on the contrary it presents signs of contraction and expulsion of liquid.

The *kidneys* exhibit evidence of grave pathological disturbance. They are increased in size and much congested. Ecchymotic spots and patches are sometimes seen beneath the capsule and throughout the parenchyma. The tubes are blocked with a granular and protoplastic material. The epithelial cells are cloudy and swollen, their contents granular, and in later stages fatty. In advanced cases the tubes are devoid of epithelial covering. The cells undergo, in fact, an acute process of degeneration and destruction.

The state of the *urine* accords with these conditions. The secretion is at first suppressed, then scanty, of high specific gravity, albuminous, and containing casts — epithelial, granular and hyaline; and ultimately, in prolonged cases, abundant in quantity, watery and devoid of albumin. The proportion of saline materials is greatly diminished in the urine of cholera, and of urea somewhat. Indican is a conspicuous constituent (Crombie). Bright's disease is a rare sequel of cholera. Temporary glycosuria is sometimes met with. The *bladder* is generally found empty and firmly contracted in cases fatal during the early stages of the disease.

The *circulatory system and blood* undergo serious and characteristic changes in cholera.

The heart is not altered in structure, but in some cases hæmorrhagic spots and patches may be observed. The right cavities are generally distended with dark tarry blood; the left, as a rule, are empty. The distension extends into the venæ cavæ and into the pulmonary arteries as

far as the lungs. In a considerable proportion of cases white clots are found in the right cavities, and extending into the pulmonary arteries: detached thrombi have also been found in the latter. Dr. Wall concludes from clinical and post-mortem observations that thrombosis is a common incident of the collapse stage of cholera, and that the clots in the heart and vessels undergo liquefaction, fragments of them sometimes remaining as pulmonary emboli and infarcts. The pulmonary veins are found empty and contracted in cases fatal during the stage of collapse. The distribution of blood in the body is abnormal, the veins and their tributaries are distended with thick dark blood, and the arteries and capillaries empty. The solid organs exhibit well-marked venous congestion. In the later (reactive) stages of the disease these conditions of the circulation undergo change; also when recourse has been had to warm saline intravenous injections — the change being towards a restoration of the ordinary distribution and balance of the blood.

The physical, chemical and microscopic conditions of the blood have been made the subject of elaborate research. Three osmotic processes appear to exist during the progress of choleraic disease: 1st, an exosmotic effusion from the vessels into the intestinal canal; 2nd, an exosmotic current from the corpuscles into the surrounding fluid; and, 3rd, an endosmotic transit of fluid from the tissues into the vessels. By these processes the blood becomes profoundly altered physically and chemically. The outflow of constituents has been determined by Schmidt to take place in the following order: the water transudes before the solids of the serum, the inorganic before the organic solids, the chlorides before the phosphates, the salts of soda before the salts of potash. The same law applies to the other currents which, however, are smaller and later, and fail to replace the material which has escaped. The blood in acute cholera is therefore found to be of high specific gravity, very dark and inspissated, and deficient in water and salts. Cells and albumin are in excess, but authorities differ as to the amount of fibrin factors and the coagulability of the blood. The amount of oxygen in the blood cells is seriously diminished. The blood regains its brightness on exposure to air in thin layers, and on contact with the intestinal discharges (Parkes). Urea has been found in it in cases fatal in the algide stage. Detachment of the epithelium of the vessels and adhesion of the blood to the denuded surface have been described (Thudichum).

An excess of leucocytes was discovered by Virchow, and confirmed by Lewis and Cunningham, who found the red corpuscles diffluent; they observed that the leucocytes underwent a series of changes — becoming granular, rounded, still, and then vacuolated — and ultimately discharged their granular contents. The empty cell walls constitute, according to these observers, the peculiar hyaline vesicles which are found in the evacuations. Much of the protoplasmic granular material which forms so large a proportion of the latter is held to be derived from the blood, through the agency of leucocytes, which undergo after transit the changes described. No special organism or material of the nature of virus or

poison has been detected in the blood of cholera either by the microscope or by chemistry.

The *lungs* in a case of death in the collapse stage are found to be light, dry and shrunken. There is a deficiency both of blood in the vessels and of air in the alveoli. These are the characteristic cholera lungs; but in later stages they may be congested, œdematous or collapsed. The *pleuræ* are usually healthy.

The *brain* and its membranes exhibit venous congestion. Signs of meningitis are sometimes present in advanced cases.

The *tissues* are dry, doughy, and shrunken from removal of water. The muscles are also dry and contain an unusual amount of urea. They are sometimes found ruptured.

Theory of Cholera. — The phenomena observed during life and the appearances seen after death undoubtedly indicate that the choleraic process is due to the entry into the system of a poison which causes, in the first instance, violent functional disturbances; then sets up serious organic disorders, and finally results, if life be prolonged, in important structural changes. This poison has not as yet been isolated, but there is every reason to believe that it is of organic constitution, and a strong probability that it is elaborated either within or without the body by a microbe, and recent research points to this microbe being a vibrio. The early incidents of cholera cases — more particularly the varying duration of the incubative stage, the general occurrence, but frequent absence, of initial signs of intestinal irritation and nervous disturbance and depression — would suggest that the disease may be due either to ingestion of a poison elaborated elsewhere, in which case the invasion would be sudden, and the effects depend on the dose; or to the reception into the intestinal tube of a microbe under circumstances favourable for its multiplication; in the latter case symptoms of intestinal derangement, of longer or shorter duration, would precede the general poisoning by absorption of the elaborated product.

This theory would also account for the failure to find a specific organism in a certain proportion of cases — a fact attested by good authority — as well as for isolated outbreaks on board ship and elsewhere, which might be due to conveyance of a limited quantity of the elaborated product.

The phenomena of cholera, especially of its later stages, constitute a remedial reaction; and the disease has with plausibility been likened to a febrile paroxysm with a severe and prolonged algide stage. Cases and outbreaks of malarial fever have been observed which it was found almost impossible to distinguish from cholera. On the other hand, in some cases and outbreaks of the latter disease the febrile phenomena assume a marked prominence. The poison seems to exercise a special influence — deleterious and destructive — on the epithelial elements of the intestinal and urinary tubes, and on the gland sacs and follicles of the former; but a strong impression on the nervous system, leading to contraction of arterioles and disturbance of the balance of the circulation, with pre-

ponderance towards the venous side, is a very early effect of the poison in the blood, which soon undergoes important dynamical, organic, and chemical alterations. Many of the later incidents of cholera are due, no doubt, to absorption from the tubes and tissues of secondary poisons of bacterial or degenerative origin. The theory that the intestinal disturbance is sufficient to account for all the other phenomena of cholera as secondary and consequential effects is no longer tenable; and the choleraic process cannot be satisfactorily explained otherwise than as the effect of one of those organic poisons which constitute a very early stage of decomposition of proteids, or result from the metabolism of these by the agency of micro-organisms.

When the virulence of the poison has been spent, or its removal effected, the primary disturbances set up by it are very soon and completely recovered from. The secondary changes occurring during the stage of reaction are more serious and prolonged; but these likewise very seldom leave permanent structural defects.

Diagnosis. — The maladies which most closely resemble cholera are ptomaine poisoning; mushroom poisoning; certain varieties of diarrhœa; and some rare malarial fevers, with intestinal complications, and a profound and prolonged algide stage. The identification of Asiatic cholera turns upon clinical, epidemic and bacteriological considerations. The clinical features which mark an ordinary case of cholera are: the copious, painless passage of watery motions, devoid of bile colouring, resembling rice water and exhaling a characteristic odour; the profound nausea and frequent vomiting of watery material; the suppression of urine; the muscular cramps; the cyanosis and shrinking of skin; the cold breath and whispering husky voice; the dyspnœa and restlessness; the prostration, torpor and failing pulse; the cold sweats and depression of the surface temperature, with a tendency to rise of internal temperature. These constitute a group of symptoms which may be imitated, but are seldom if ever identical with those of any other flux. If cholera is known to prevail in the locality or neighbourhood, or circumstances permitting or favouring importation exist, suspicion naturally attaches to all bowel complaints; even if they do not present the extreme form just pictured. Similarly, cases of diarrhœa, however mild, arising in the midst of an epidemic of cholera are viewed with apprehension. If numerous seizures occur in groups, and the mortality equals or exceeds 50 per cent, the identification is rendered more easy and certain. Cases of ptomaine and muscarine poisoning, which most resemble cholera, generally occur singly, or in small groups; and usually follow the eating of fish, shell-fish, tinned provisions or mushrooms; fragments of mushroom may be found in the stools. The association with prevalent malarial fever, the absence of epidemic cholera in the place or vicinity, the periodicity, the better marked febrile stage, the lower mortality, and the amenability to quinine, serve to distinguish the cases of malarial fever which, in the algide stage, may assume a choleraic character. The suppression of bile and urine, the cyanosis, cramps, collapse and cold, and the high mortal-

ity, are the chief circumstances which distinguish cholera from other diarrhœas. The bacteriological conditions are also important. The detection of Koch's vibrio in the evacuations constitutes, according to our present knowledge, a means of separating cholera from every other disease. The negative, however, is not true. In a certain, though small, proportion of cases the vibrio cannot be found. It is also alleged that several varieties or species of spirillum, exhibiting different morphological and physiological characters, develop in the intestinal discharges of cholera (Cunningham). These matters are at present the subject of keen and searching investigation, and a detailed discussion of them would be premature and unprofitable. [*Vide* section on Bacteriology.]

Prognosis. — The death-rate of cholera varies with the character of the epidemic and the period of the outbreak. Fifty per cent may be accepted as an average death-rate, but it is often exceeded in specially severe outbreaks, and in the early stage of any outbreak. The very young and very old succumb more readily than the middle aged; sucklings are seldom attacked. Women are rather less frequently seized than men; pregnancy is a dangerous complication. Organic disease of the kidneys is a specially unfavourable condition, and organic disease of the liver almost equally so. Drunkards are bad subjects of cholera; so are persons of feeble and damaged constitution; ill health, however caused, is an unfavourable introduction to the choleraic struggle. During the progress of a case signs of good or evil omen are observable at every step.

Evil signs, in the order of the stages, are — Sudden seizure, early prostration, early stupor, quick advent of collapse, restlessness and fighting for breath, failing pulse, great depression of temperature, prolonged cold stage, hyperpyrexia, severe abdominal pain, blood in vomit and stools, persistent suppression of bile and urine, permanent muscular contractions, jaundice, lung complications, recurrent purging and vomiting, delayed restoration of body heat, typhoid symptoms and indications of uræmia or cholo-uræmia, insomnia and delirium.

Good signs are — Maintenance of pulse during collapse, moderate depression of temperature, early and not excessive reaction, return of colour in the motions, cessation of cramps, restoration of urinary secretion, resumption of warmth and dryness of skin and normal colour and plumpness of face, quiet breathing, tranquillity, sleep.

The violence of vomiting and purging in the early stages are not necessarily indicative of a severe seizure, but their persistence is apt to result in delayed convalescence or fatal exhaustion.

Treatment. — The fact that about one-half of those attacked with cholera recover, with or without treatment, indicates that processes antagonistic to the poison and curative of its effects arise within the organism, and are effective in that proportion of cases. What the precise nature of these processes may be it is impossible, in the present state of science, to affirm. Whether the poison of cholera lose its power by lapse of time, or be diluted, eliminated, or destroyed; or whether there be formed in the tissues or blood or intestinal tube some antagonistic principle — an

alexin or antitoxin, to adopt the language of modern bacteriology — we know not: in our ignorance of the process of natural cure it is impossible to formulate a rational system of treatment in imitation and furtherance thereof. Two principles may, however, be confidently stated, namely, (1) that it is obviously irrational and improper unduly to interfere with or thwart processes which, though apparently morbid and injurious, result, as a matter of fact, in restoration to health in a moiety of seizures; and (2) that, in estimating the value of any system or method of cure, the law of natural and unaided recovery must be taken into account, allowing for the character and period of the outbreak.

Prevention. — The sanitary measures by which a community may be protected from cholera, by which its entry may be prevented, its spread controlled, its incidence and mortality minimised, are discussed in the section relating to the history and etiology of the disease considered epidemiologically.

Personal prophylaxis, however, constitutes an important item of the treatment of cholera as affecting individuals. Certain circumstances and conditions have been recognised as rendering persons specially liable to attack. The chief of these are — bodily fatigue, mental worry, panic, disorder of stomach caused by consumption of raw fruits and vegetables (melons, cucumbers, and the like have been specially blamed), decomposing animal food, particularly fish and shell-fish, excessive use of alcohol, drinking impure water or milk, the use of purgative medicines especially salines, exposure to cold, and generally anything tending to depress the general vigour and derange health. The conduct and regimen necessary to avoid these risks need not be detailed.

On grounds of reason and experience the most efficient preventive of cholera, both for individuals and bodies of men, is removal from the infected locality to another place, higher and drier if practicable, where the disease is not prevalent. New comers to infected places are specially prone to attack. Although the disease does not appear to be often, if ever, communicated directly from person to person, avoidance of association with the sick is advisable, because such association may involve exposure to the morbific conditions surrounding the sick.

Chemical disinfection of excreta and discharges, and of articles which have been soiled thereby, is obviously advisable; and the free use of such agents as carbolic and sulphurous acids highly commendable. Protection against attack by the administration of drugs, such as quinine and the mineral acids, has been tried without satisfactory results.

Anticholeraic Vaccination. — Various attempts have been made to render the system immune to choleraic infection by the injection of antitoxins. The latest is the method devised by M. Haffkine. It has been amply proved that the use of the weak virus, prepared by his method, mitigates, both in animals and men, the local and general effects subsequently produced by the strong; and that an immunity against the latter may be thus produced. Extensive inoculations of human subjects have been carried out by M. Haffkine in India. Upwards of 42,000

persons have been vaccinated without accident or harm. Evidence has been gained that recent inoculations are protective; but the experience is as yet too meagre and incomplete to justify final conclusions as to the merits and uses of the system.

Medicinal Treatment, Nursing, and Dieting. — The drugs and compounds which have been administered empirically in cases of cholera are legion. It is safe to assert that not one of them has established a claim to cure the disease. It were useless, therefore, to catalogue or discuss them. Four plans of treatment stand out prominently among others as possessing some basis of reason, and offering some promise of success; namely, the astringent, the eliminative, the antiseptic, and the stimulant. To these may be added the antispasmodic and the counter-irritative. The astringent plan contemplates the choleraic process as a hypercatharsis, and its danger as depletion; rice water evacuations being regarded as potentially hæmorrhage (Chevers). Astringents, mineral and vegetable, in combination with opium, antispasmodics and stimulants, have, in accordance with this view, been administered by mouth and rectum, in the hope that if the dangerous flux be checked, the margin of recuperative power thus saved will suffice to avert fatal exhaustion and to restore health. It is possible, however, that the results thus to be prevented or cut short — the tremendous drain of serum, corpuscles and salts from the veins into the intestinal tube, the reversal of the normal currents, and the abeyance of absorption — may have a salutary purpose, and within limits a curative function; it is doubtful whether the checking of these discharges is, as a dominant principle, a sound basis of action. Still the principle has its place in that scheme of treatment which, as we shall presently show, experience has sanctioned.

The eliminative plan, on the other hand, looks upon the flux as adjuvant — as a means of conveying the cholera poison out of the system, and seeks to aid it by administering purgatives. But, apart from the well-established fact that purgation is of itself exhausting, especially so in the early stages of cholera when it ought to be most effective and beneficial, it is questionable whether it is wise to remove materials artificially from the intestinal tube — such, perhaps, as leucocytes or their alexins, or innocuous bacteria — which may tend to neutralise or destroy the poison of cholera. As a matter of fact, Sir George Johnson's castor oil treatment has been extensively tried and found wanting. Stimulation of the kidneys by diuretics has also been tried under the guidance of this hypothesis, and found to do more harm than good.

The antiseptic plan aims at neutralising the poison in the intestinal tube, or setting up conditions there which may render its elaboration impossible. Acids and germicides of many kinds have been administered with this view; but this plan may simply result in adding poison to poison, or irritant to irritant; in hindering a process of salutary decomposition, or in destroying the leucocytes or innocuous organisms and their products which may be doing good work. Practically, the plan has failed to cure cholera.

The stimulant or restorative plan simply endeavours to avert death from exhaustion, and to sustain the flagging vital powers under circumstances of terrible depression. Alcohol, ammonia and ether administered by mouth or rectum, or hypodermically, are the favourite remedies of this class, supplemented by strong soups and nutrient enemata. Even this method is not without its drawbacks. Gastro-intestinal irritation may be increased, mischief may arise during the reactive stage, or perhaps undue disturbance of the collapse stage may be hurtful. These considerations suggest caution in the use of stimulants.

The antispasmodic plan is based on the fact that the muscles of the intestines, arterioles, bile ducts, limbs and trunk are thrown by the action of the poison into violent contraction; pain and exhaustion tending to death are thus caused. The clamping of the pulmonary arterioles, impeding the circulation and banking back the blood — hindering, that is, its aeration in the lungs, the nutrition of the brain, the action of the kidneys and skin, and promoting flux — is considered specially perilous. Warm baths, chloroform inhalation, sedative and antispasmodic drugs, nitrite of amyl and nitro-glycerine, and warm intravenous injections, have been given to relieve spasm. This treatment has proved useful as a means of relieving some symptoms.

The use of counter-irritants is intended to remove morbid action from within to the surface, where it may be less hurtful and more under control. Measures of this kind may be useful as auxiliaries.

It may be asserted with confidence that in the present state of our knowledge no single principle or plan of treating cholera has met with much success. It is possible, nevertheless, to lay down certain rules of action which, as experience has taught us, may aid the patients in undergoing the terrible struggle for life which the choleraic process entails. These will be briefly stated as they apply to successive stages of the disease.

1. *Check the Preliminary Diarrhœa.* — All authorities are agreed as to the advantage of this measure, which promptly cures mild cases and prevents others from becoming dangerous. Combinations of opium with astringents and antispasmodics constitute the favourite formulæ. The remedy may be given in pill or mixture. The "cholera pill" of India consists of opium, assafœtida and black pepper. Goodeve used acetate of lead and opium. Chevers preferred vegetable astringents. The cholera tinctures, which have often proved so serviceable, are generally composed of laudanum or liquor opii sedativus with catechu or kino, compound tincture of lavender or cardamoms and chloric ether. Chlorodyne, with or without brandy, according to the state of the patient, is an admirable remedy of similar composition, fulfilling the same end. The dose and frequency of repetition must depend on the age and condition of the patient, the degree of irritability of the stomach, and the effect of the remedy. The practitioner must exercise a careful observation and judgment on these points; it is inexpedient to lay down precise rules or formulæ. If the stomach be very irritable a

mustard poultice or chloroform should be applied to the epigastrium, and lumps of ice given to suck. If medicines are still rejected the hypodermic injection of morphia may be resorted to. It must be clearly understood that the treatment now recommended is applicable to the preliminary and evacuatory stages only. When collapse has fairly set in opium and astringents must be stopped; for absorption being now in abeyance they are useless, and in the stage of reaction, when absorption again sets in, they may do harm.

2. *Maintain Physical and Physiological Rest.* — The patient must be kept in bed and the evacuations received in a bed-pan. Fussy changing of clothes and bedding must be avoided. Violent rubbing, rough lifting into baths and other beds, transfer to another room or house, and, above all, a journey are dangerous. Medicines, food and stimulants should not be forced on an irritable stomach; they provoke vomiting, excite irritation, and increase exhaustion. The indication is to refrain from anything that may add to the wearing effect of a most weakening malady.

3. *Restore a Failing Circulation.* — If the pulse be maintained in the collapse the less done the better. If the pulse gradually lose volume and power, and become feeble and thready, a mild stimulant should be given — iced champagne and soda water, weak brandy and water (iced) — in teaspoonfuls, or ammonia or chloric ether well diluted. Should the pulse respond nothing further is needed. If, however, the pulse become imperceptible at the wrist, and hardly perceptible in the brachial and femoral trunks — if, at the same time, cyanosis and dyspnœa are well marked — the condition is one of imminent danger. Hypodermic injections of sulphuric ether, or cautious doses of nitrite of amyl or nitroglycerine, followed up by champagne or brandy, may restore the pulse; but nothing effects this so speedily and surely as the intravenous injection of warm saline solutions. Sixty grains of sodium chloride and 30 of sodium carbonate are dissolved in 1 litre (about 35 ounces) of distilled water. The fluid should be sterilised by boiling, and injected slowly at a temperature of about 98·4° F., with strict antiseptic precautions, into one of the veins of the arm. A reservoir containing five or six litres should be kept ready and placed on a stand about four feet above the level of the patient's head. The injection flows by gravitation through a flexible tube, by pressure on which the rate of flow is regulated. The rate of entry should be slow, say one litre in twelve minutes. The amount injected will depend on the effect; one to three litres may be required in different cases to restore the pulse (Wall).

In most cases the fluid leaves the blood-vessels and passes into the intestinal tube, and the symptoms of collapse recur. They may nevertheless be removed again and again by a repetition of the injection, and in some cases a permanent cure results. Experience has, however, shown that the proportion of recoveries has not been materially increased by the use of saline intravenous injections. Still, distress is for the time relieved, life is undoubtedly prolonged, some cases seem to be saved; and in the face of impending death anything that offers the faintest hope of rescue is

justifiable. Intravenous injection of milk and transfusion of blood have been tried without much benefit, if any. It has been sought to restore fluid to the blood by injecting saline fluids and plain water into the cellular tissue, peritoneum, bladder and rectum. No harm has resulted from such procedures, and little if any good. The fluid is readily absorbed, but as readily passes away through the intestines. It is possible that these artificial means of restoring water and salts to the blood simply keep the exosmotic current flowing, which might otherwise cease or be reversed through the altered specific gravity of the blood. It has also been sought to remedy stagnation of the circulation by the warm bath and mild rubbing of the limbs. These measures should be applied with the utmost gentleness. Rubbing with dry powdered ginger is a routine practice in India; clamminess and moisture of skin are thus removed, and mild stimulation of the cutaneous vessels and nerves attained. The practice, if cautiously followed, does no harm, and probably does some good.

4. *Conserve the Body Heat.* — The great depression of surface temperature which takes place in the collapse stage of cholera is no doubt due to many causes — amongst them the direct effect of the poison on the nerve centres, the disturbance of circulation, and the loss of fluids from the intestinal and cutaneous surfaces. It is probably more a sign than a cause of exhaustion. Still, it seems desirable to prevent the evitable escape of body heat. The temperature of the room should not be allowed to fall below 70° F., and the air in the immediate vicinity of the patient should be warmed by a few hot bricks or bottles: this is better than loading him with bedding. Ventilation should be free, but draughts avoided; in hot climates the punkah should be gently pulled. The surface should be kept as dry as possible, and gentle wiping with soft cloths or rubbing with dry ginger powder resorted to. The warm bath also tends to restore the surface temperature.

5. *Allay Thirst.* — The craving for fluids in cholera is astonishing, and ought to be gratified; but large draughts excite violent vomiting and so lead to exhaustion. Giving lumps of ice to suck is perhaps the best method of quenching thirst; still small quantities of iced soda water, iced champagne and soda, barley or arrowroot water, milk and soda, or teaspoonfuls of cold jelly or clear soup may be administered at short intervals. The injection of fluids into cavities and tissues tends indirectly to fulfil the same indication.

6. *Relieve Distress and Pain.* — The cramps undoubtedly constitute the most painful symptom of cholera, and it is not easy to relieve them. Probably the opiates administered in the early stages exercise an analgesic effect. Hot applications, the warm bath, gentle frictions with anodyne liniments, or even moderate counter-irritation with chloroform, turpentine, or mustard may be tried; but nothing relieves cramps so well as moderate and intermittent chloroform inhalation. Camphor has been recommended internally, externally and hypodermically. For the severe abdominal pains which are sometimes met with, hot applica-

tions and counter-irritation with chloroform or mustard give relief. In early stages a moderate dose of liquid extract of opium may be injected over the seat of pain. The relief of general distress is best accomplished by warm baths and intravenous injections, but these must be used with caution and judgment. Dr. Lauder Brunton has recommended the hypodermic injection of atropine in cholera, but rather on the ground of its known antagonism to muscarine, which causes symptoms closely resembling cholera, than on account of its anodyne properties. Sufficient trial has not as yet been made of the drug to warrant its confident recommendation.

7. *Check Persistent Diarrhœa.*—Persistent or recurrent purging, causing exhaustion and delaying recovery, sometimes occurs in the stage of reaction. Vegetable astringents or mineral acids may be given in small doses well diluted, but the large, warm, astringent rectal injections recommended by Catani are more efficient. Twenty grammes (308 grains) of tannic acid and as much gum-arabic are dissolved in one litre of water. The injection is made very slowly by gravitation to such amount as the patient can comfortably bear. Blood heat is the best temperature, and the material should be retained as long as possible (Wall).

8. *Check Irritability of Stomach.* — This may be manifested as obstinate vomiting or incessant hiccough; or signs of severe gastritis, induced perhaps by injudicious administration of food and stimulants, may be present. There is no special cure for this condition, which is to be treated on ordinary principles.

9. *Reduce Excessive Temperature.* — It is extremely difficult to fulfil this indication; and this is the more to be regretted inasmuch as the hyperpyretic form of cholera is very fatal. Ice sucking and the slow injection of bulky cold enemata may be tried; antipyretics should be avoided. Tepid baths gradually cooled may be resorted to, but great caution is necessary in any such adventures.

10. *Restore the Secretion of Bile and Urine.* — As regards the bile, very little if anything can be done to promote its secretion or evacuation; in most cases, fortunately, nothing need be done. Usually, when the cold stage has passed and spasmodic closure of the ducts is relaxed, the flow is resumed. Sometimes the outpouring of the imprisoned bile is excessive and gives rise to bilious vomiting. In those cases in which the function of the liver has been so much impaired that a watery material is poured into the ducts instead of bile, no means have been discovered of correcting the condition. Calomel has been given in large and small doses, with the intention of stimulating the secretion and discharge of bile. Large doses are undoubtedly injurious, and small doses, even when combined with soda, are of very doubtful value.

The restoration of the urinary secretion is a more important object; its prolonged suppression is fatal. Dry cupping, hot fomentations and poultices may be applied in cases of delayed return; and water, milk and water, barley water, etc., freely given. Diuretics should be

avoided. When head symptoms are severe and the bowels confined, mild enemata, or even a little castor oil emulsion, may be given; but great caution is necessary in the use of such measures. The bladder should be examined by catheter occasionally if necessary.

Special symptoms, complications, and sequelæ are treated according to the appropriate methods, always bearing in mind the great strain to which the system has been subjected by the choleraic process, the special danger of re-exciting gastro-intestinal irritation, or of putting additional stress on the damaged liver and kidneys, on whose restoration to healthy function life so greatly depends.

In most cases of recovery from cholera health and strength are rapidly regained, and the patient in a few days seems none the worse of his attack. In some cases anæmia, emaciation, debility, deranged stomach and bowels, and general enfeeblement and bad health of a persistent and intractable description, ensue. Change of air is the best means of combating this state. Tonics and careful dieting and regimen are also necessary.

The *dieting* of cholera subjects is a difficult task. The simplest possible liquid food should be given in small quantities during the attack, and ordinary food be very gradually resumed during convalescence. It is needless to catalogue here the articles of diet which may be administered [*vid.* art. on "Dietetics and Sick Feeding"]. These directions must be left to the discretion of the practitioner, but fatal relapses have not infrequently been caused by injudicious dieting. Finally, it may be asserted with confidence that, although no "cure" of cholera has as yet been discovered, careful attention to the state of the patient with a view to the fulfilment of the needs which I have indicated above, will relieve much suffering and save many lives.

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PLAGUE

Synonyms. — Oriental Plague, Bubonic plague, *Pestis*, *Pestilentia:* Pali plague or Mahamurrie (in India). The Black Death (fourteenth century in Europe).

Definition. — An acute infective febrile disease, accompanied by inflammation of lymphatic glands; partly miasmatic, partly communicable, caused by a micro-organism, the bacillus pestis.

History of the Plague. — The first historical notice of a disease like bubonic plague records its occurrence in Libya in the third century before Christ, or earlier; but this notice is only contained in a fragment from the writings of a much later physician, Rufus of Ephesus (about 100 A.D.), who also speaks of its occurrence in his own time in Libya, Egypt, and Syria. Whether it was clearly known to the classical Greek writers on medicine is doubtful, but Aretæus speaks of *βουβῶνες λοιμώδες*, or pestilential buboes. The plague of Athens described by Thucydides was apparently not this disease; nor was the destructive pestilence of the reign of Marcus Aurelius alluded to by Galen. We meet with bubonic plague again, however, in the great Plague of Justinian, which started from Egypt 542 A.D., and spread over a large part of Europe; it was described in Gaul as *lues inguinaria.* Epidemics succeeded one another in this and the succeeding century; but after that time it is difficult to follow the track of plague. Many European pestilences are spoken of in mediæval histories, which may or may not have been bubonic plague; no sufficiently clear record remains.

In the fourteenth century a new era began. All previous European plagues could be traced back, directly or remotely, to Africa, especially to Egypt; but now a new epidemic invaded Europe from Asia by way of the Crimea and the Black Sea, its origin being referred to Cathay or China. This terrible pestilence, afterwards known as the "Death," or the "Black Death," appeared in Southern Italy in 1346–47, and made its way over the whole of Europe. It reached England early in 1348 and for several, probably five or six years, was prevalent in various parts of the country. Scotland and Ireland were affected in their turn; and no country in Europe seems to have escaped. A second epidemic occurred in 1361, and a third in 1368. The details of this great calamity have often been dwelt upon by historians and cannot be given here. It is calculated by Hecker that 25,000,000 of persons, one-fourth of the population of Europe, died of this disease. Although it has been doubted whether this was the true bubonic plague, as the first epidemic presented some peculiar features, yet it must now be accepted that the Black Death was that disease in a peculiarly malignant form.

The great importance of this fact in epidemic history is that from this time forth, whether previously or not, plague was established as an endemic disease in England and other parts of Europe; though it

is quite possible that, as Hirsch and others think, fresh importations of the virus from the East took place from time to time. The successive epidemics in Britain through the fifteenth, sixteenth, and seventeenth centuries are fully recorded in Dr. Creighton's *History of Epidemics in Britain*. Finally they culminated in that called the Great Plague of London in 1665, in which about 70,000 persons died, and which extended widely over the country. Soon after that the disease vanished, never to recur on English soil.

During these centuries most countries in Europe suffered from repeated epidemics. It was noticed that the epidemic wave passed on the whole from East to West, or from the Mediterranean countries northward; which led to the belief that many European epidemics were derived from more persistent foci of plague in Turkey, the Levant, and Egypt. Hence the system of quarantine, by sea and land, was introduced to stem the tide of infection. This belief, which is that of many epidemiologists, receives support from the fact that the disease died out earlier in Western than in Eastern Europe. Holland, France, Spain, and Italy became exempt, with one notable exception, a little later than England — about the end of the seventeenth century. Eastern Germany suffered somewhat longer, while in Poland, Russia, parts of the Austrian Empire, and the Danubian countries, epidemics were repeated throughout the eighteenth century. There was thus a general eastward recession; the chief exception to which was the great epidemic of Southern France, 1720–21. This was generally attributed to the arrival, in the port of Marseilles, of a ship from Syria infected with plague, which then spread to the populous and insalubrious city. The invasion of islands like Sicily and Malta in the eighteenth century was clearly due to the same cause, namely, to a contagion imported by sea.

During the first half of the nineteenth century plague prevailed in Turkey, and made occasional advances into the Danubian countries, to the shores of the Adriatic seas, and to the south of Russia. Being still almost constantly present in Egypt and Syria, it seemed to be a disease peculiarly of the Eastern Mediterranean, and thus acquired the name of Levantine Plague, which has lasted to our day; and the strictest precautions were still taken in all the Mediterranean ports to prevent its invasion.

Finally in 1841 plague left Europe by its Eastern gate, Constantinople; and in 1843–45 it became extinct also in Syria and Egypt, so that the old Levantine Plague seemed to have entirely vanished. It is clear, however, that in Asia Minor it did not die away, but only receded eastward. At the beginning of this century, the Caucasus, according to Tholozan, was the centre from which epidemics radiated; but in the latter half of the century that centre has been shifted to the mountains of Kurdistan.

Good authorities still held that the disease was probably not extinct; and these suspicions were confirmed by accounts received at Constantinople, in 1853, of an outbreak in the Azir district of Arabia already mentioned: this outbreak has been followed repeatedly by others at intervals

of some years; the last was in 1889. In 1858 the same disease was heard of in Benghazi, where it must have prevailed at least two or three years before; and there it appeared again in 1874, and possibly again later. The plague also in the province of Tripoli so lately as 1837, has recurred in the form of epidemics which were relics of the former wide distribution of plague along the whole northern coast of Africa.

The more recent accounts of plague in the Kurdistan district, on the frontiers of Turkey and Persia and Mesopotamia, begin with 1863; but it must not be supposed that this was the first appearance of the disease in that part of the world — Baghdad and the neighbourhood had suffered severely at the beginning of the century, and for all we know to the contrary, for centuries before that.

The chief known recent epidemics of Persia and Kurdistan were in 1863, in 1870–72, and in 1876–77; in 1877 a terrible epidemic occurred also in the town of Resht on the Caspian, which is an important occurrence in relation to the epidemic of 1878 on the Volga. The latest recorded appearance of plague in Persia was in 1885; but it was probably not the last.

In Mesopotamia (Irak-Arabi), from 1856 onward for several years, there prevailed what is now known to have been the mild form of plague. In 1867 a definite epidemic was recorded; in 1873–74 another extending over a much wider area; and in 1876–77 one still more extensive, and very severe. A further outbreak occurred in 1880–81, which is said to have destroyed one-quarter or one-third of the population; and another in 1884.

The above short record is of interest as showing how plague may extend its area in successive epidemics; and also as leading up to the comparatively small epidemic on the Volga in 1879, which caused so much alarm.

As has been shown, in the years 1876 and 1877 the plague was very active. In June 1877, and also in the two years following, a febrile malady accompanied by buboes appeared in Astrakhan on the northern shore of the Caspian, a place in direct communication with Resht on the Persian shore, and it extended to neighbouring villages. Though it was of a mild type and caused but few deaths, it was certainly the mild or minor form of plague. In October 1878, a similar but more severe epidemic broke out in the Cossack settlement of Vetlanka, 130 miles up the Volga; and by December it assumed the character of the most virulent plague. The epidemic lasted in this village till 24th January 1879; but in December it had already spread to other villages, in which nearly every patient died. The last death in the district occurred on 9th February. Though affecting a small population it was very fatal, causing 382 deaths in a population of 1700. The mortality was nearly 90 per cent.

This is the simple history of the epidemic which caused a panic through Europe. It is easily explained when we see its filiation with the mild epidemic of Astrakhan and the severe one of Resht; and the

general prevalence of plague in Persia in previous years. A minor epidemic in 1877 at Baku, on the western shore of the Caspian, furnishes another link. Why the disease was so mild in Astrakhan and so virulent in Vetlanka we cannot tell; but a like sudden development of the severe out of the mild form of the disease is frequently observed.

History of Plague in India. — Plague has been little known in India; the climate generally seems too hot for it: three centres have, however, been known in this century. In 1815 an outbreak, following a famine, occurred in Cutch, Guzerat and Kattywar. The next year it reappeared, but went away in 1820. In 1836 an epidemic which broke out in Pali in Rajputana became known as the Pali plague, but it ceased in 1837. In a different locality, the districts of Gurwhal and Kumaon on the south-west of the Himalayas, a disease known locally as Mahamurrie (which is undoubtedly bubonic plague) has recurred several times since 1823. The last great epidemic was in 1876–77, but it recurred in 1886 and 1888. No connection can be traced between the above-mentioned localities of plague, nor between them and any other.

In 1883–84 a malady was observed in Candahar (Afghanistan), which presented some features of plague, but was not certainly identified.

History of Plague in China. — The first definitely known epidemic of plague in Yunnan was about 1860; but it is believed to have existed there at least since 1850, and probably long before, as it has all the characters of an endemic disease. It is said to have recurred nearly every year up to 1893. In Pakhoi it is also frequent, but was absent from 1884 to 1893. Some think the epidemics of Pakhoi were derived from Yunnan. It is impossible to trace the derivation of the disease from any other district. From Pakhoi it must in some way have found its way to Canton, where it broke out in 1894. Dr. Rennie of Canton thinks it passed by land, since in 1891 a severe epidemic occurred in the district of Kaochao, lying to the north of Pakhoi; and in the spring of 1894 it prevailed in towns to the south of Canton. From Canton to Hong-Kong it was carried by numerous persons suffering from the disease, or in the stage of incubation.

General Pathology of Plague. — Plague occupies an intermediate position between the miasmatic or malarial diseases proper, such as ague, and the true contagious fevers; there is clear evidence that its virus may be acquired both direct from the soil, and from infected persons and objects above the soil. It will be convenient, therefore, to consider it in this twofold relation, as an endemic soil-disease and as a communicable epidemic. Under both conditions its existence and propagation are explicable by the recent discovery of a micro-organism.

The Bacillus of Plague. — The phenomena of plague can hardly be accounted for except on the hypothesis of a living organic cause, one capable of living in the human body, and also in some way outside the body also. Great interest, therefore, attaches to the recent discovery, in Hong-Kong, by Kitasato, confirmed by Yersin, of a micro-organism

which seems to fulfil all the conditions required by the problem, and is probably the specific cause of the disease.

Kitasato found in the bodies of patients with plague a short, rather thick bacillus, which stains, with various dyes, in such a way that the poles are deeply coloured, while the central part is pale; thus it somewhat resembles a diplococcus. Yersin's description precisely corresponds with that of Kitasato. This bacillus may be grown on ordinary cultivation mediums — especially agar-agar, with glycerine, blood serum, and bouillon — temperatures from 97° to 102° F. being the most suitable. It is killed in thirty minutes by a temperature of 170° F., and in a few minutes by 212° F. According to both observers the bacillus is most abundant in the lymph glands; the pulp of softened buboes is indeed little more than a pure cultivation of the bacillus; it is almost equally abundant in the spleen. But few are found in the blood, and then chiefly in very severe cases of plague (Yersin). Kitasato detected them in the blood of twenty-five out of twenty-eight patients, but says that the detection is difficult, and, except in the hands of a skilled observer, does not furnish a satisfactory means of diagnosis. Cultivation from the blood, however, is more satisfactory.

Inoculation of matter from buboes into rats, mice, guinea-pigs, or rabbits gives them a febrile disease (temperature 105° F., Kitasato), fatal in from one to five days. The bodies show characteristic enlarged glands, and bacilli are present in large numbers in the glands and spleen, and a few in the blood. Yersin passed the disease by inoculation from one animal to another with increasing virulence. Inoculation of cultures of the bacillus produces the same result, and bacilli are found in the organs after death. It is thus clear that the organism is the cause of the disease in animals, and that this disease is the same as the human disease. The bacillus thus fulfils all the conditions required to prove it to be the true pathogenetic organism of plague.

The channels of reception of the bacillus are, according to Kitasato, the respiratory organs, the digestive tract, and inoculation. According to Yersin rats and mice, especially the former, fed with fragments of organs of animals dead of the disease acquired plague, and died with characteristic lesions and bacilli in their organs. It is also stated that bacilli are found in the fæcal dejections of patients, showing a mode of infection in plague previously unsuspected: indeed the bacillus is not known to leave the body by any other channel. Yersin established *contagion of plague* by keeping inoculated rats and healthy mice in the same place. All the latter, as well as the former, died with numerous bacilli in their organs.

Under certain circumstances a remarkable diminution of virulence of the bacillus was observed by Yersin. Some colonies in cultures were observed to grow much more rapidly than the others, and if cultivated separately were found to be much diminished in virulence. Bacilli obtained from convalescent patients were also of comparatively low virulence. These observations are interesting as bearing on the spontaneous decline in virulence and the cessation of plague epidemics.

Ectogenic Existence of the Bacillus. — Yersin was able to cultivate and isolate a bacillus from earth of an infected house, four to five centimetres below the surface, which precisely resembled that from buboes, but was not virulent. Kitasato found in one instance that dust from an infected house communicated plague by inoculation. Yersin found that flies die from the disease, their bodies containing the bacillus; and by inoculation of material contaminated with a dead fly he conveyed plague to animals.

The conclusion is that a bacillus has been discovered capable of parasitic existence in men and animals, capable of ectogenic life, showing spontaneous variability in virulence, and thus fulfilling all the conditions necessary to explain the observed phenomena of plague.

Endemic Plague. — In discussing the existence of plague as an endemic disease, it is necessary to take into account its geographical distribution, and to some extent its history, together with the associated physical and social conditions. The localities where it is now known to occur, or to have occurred within the last twenty years, are as follows: —

(1) In the district of Benghazi (the ancient Cyrenaica), in the province of Tripoli, Northern Africa, the most westerly station now known; last definitely recorded in 1874.

(2) The district of Azir or Assyr, in South-western Arabia, bordering on the Red Sea, as lately as 1889.

(3) A large area in Asia, comprising Persian Kurdistan and adjacent parts of Persia, Turkish Kurdistan, and parts of Irak or Mesopotamia on the banks of the Tigris and Euphrates, including Baghdad. From this area it has extended to Northern Persia on the shores of the Caspian (Resht) in 1877, to Baku on the western, and Astrakhan on the northern shore of that sea; and up the Volga to the village of Vetlanka and its neighbourhood in 1877–79.

(4) The districts of Kumaon and Gurwhal in the north-west of India, on the slopes of the Himalayas, as lately as 1888.

(5) In Southern China, the mountain district of Yunnan and the seaport Pakhoi on the Tonkin Gulf. Apparently by extension from Pakhoi, plague has in the last two years invaded Canton and Hong-Kong in Eastern China.

The five localities above named appear to be independent centres of the disease, since no communication can be traced between them; and plague is not known to exist in any other part of the world.

These localities are all in the temperature zone, with the exception of the Azir district and Pakhoi, which lie just within the tropics; but they have hardly another physical feature in common. Plague prevails in Benghazi on a rocky plateau overlooking a marshy district liable to inundation; on the banks of the Tigris and Euphrates, and on part of the shores of the Caspian in low and marshy situations. But the mountains of Kurdistan are 5000 to 6000 feet high; and the Himalayan seat of plague approaches 7000 feet above the sea; while in Yunnan the disease is said to occur only at elevations of from 1200 to 7200 feet. These facts show the old belief that plague prevails only in marshy and

malarious districts to be unfounded. In fact mountain districts are perhaps the most persistent foci of plague now known.

The social conditions of these localities are important, and will be referred to presently.

Endemic Plague as a Soil Disease. — In all the places where plague is endemic, there is reason to believe that the virus resides permanently in the soil, and that human beings acquire it thence by certain channels of communication. Plague is therefore partially, though not wholly, a miasmatic or soil disease. It differs from malarial disease in that it exists only in the soil of inhabited places, and has never been acquired from mere telluric conditions. Since the living virus is a bacillus which exists in the affected subjects, it will pass from them back into the soil, and a mutual relation be thus established. The soil theory of plague is a popular belief in some parts of the world. It was dimly perceived by many older writers (by Boghurst in the seventeenth century); but was obscured by other less tenable hypotheses of infection of the air and epidemic constitutions. It was clearly recognised by Dr. C. R. Francis as the explanation of the Indian plague of Kumaon in 1853. It was suggested as possible by Liebermeister in the article on Plague in Ziemssen's *Cyclopædia of Medicine*, and adopted, subject to further evidence, by myself in the *Encyclopædia Britannica* and elsewhere: but it was first definitely formulated, with the aid of Pettenkofer's theory of soil water, by Dr. Creighton in his *History of Epidemic Diseases*. It is apparently not held by most epidemiologists.

The arguments in favour of this view are somewhat as follows: —

(1) The remarkably limited geographical distribution of plague, so widely different from that of diseases caused by a floating or purely personal contagion, is hardly consistent with any other hypothesis.

(2) In localities where the disease is permanently established animals living underground are often affected in a peculiar way. Usually before the outbreak of an epidemic such animals, especially rats, perish in large numbers. They come out of their holes evidently very ill, and die, or are found dead under ground; so that this phenomenon is considered by the people in India and China, where it has been chiefly observed, as the sign of a coming epidemic. Recent observation in China has shown that the rats suffer not merely from poisoning, but from true bubonic plague. They have buboes, and their organs contain immense numbers of the plague bacilli. It cannot, therefore, be doubted that the virus exists under ground before it affects human beings. In some countries other animals are said to be affected, but this is less certain.[1]

(3) Within an endemic area of plague the disease often occurs year after year, or in successive epidemics, precisely in the same spots, even in the same houses; and springs up simultaneously in several independent

[1] In the older European epidemics it seems doubtful whether this death of rats was actually observed. The old books contain general statements of the same kind regarding animals which live in the ground, but they have the appearance of being traditional, and borrowed from the Arabian writers, especially from Avicenna, who is very copious on this point.

foci. In London in 1665 it was said the disease "fell upon several spots of the city and suburbs like rain."

(4) Of places apparently under the same conditions, and in free communication with one another, one is repeatedly affected, the other never. Dr. Francis observed in India two villages on the same mountain, with the same aspect, scarcely 500 yards apart, of which, at every visitation of plague, one always escaped, the other suffered. In old days, again, it was observed in Egypt that Alexandria might have a terrible epidemic, while Cairo entirely escaped: in another epidemic the converse relation might obtain; and this in spite of unchecked communication.

(5) In cities, where a notable part of the population lives on the water in boats and barges, it has more than once been noted that such persons have entirely escaped the plague. It was so in London in 1665; and recently in Canton, where 250,000 people live and sleep on the water, this part of the population enjoyed almost complete immunity.

(6) It has often been observed that while those who live on the ground floor of a house are seized with plague, the inhabitants of the upper stories may entirely escape; so that it used to be said, "Plague does not go upstairs." This has been signally confirmed in the late epidemic of Canton.

(7) In a general way, the beneficial effects of local sanitary measures, as compared with mere prevention of contagion, tell in the same direction; but the bearings of these facts can only be thus briefly indicated.

It would appear from the above reasons that the endemic prevalence of plague is comparable to that of cholera or typhoid, and governed by somewhat similar laws; though in other respects it differs very much from those diseases. In the double infection of the soil and the organism it resembles anthrax. Along with infection of the soil there appears to be a passage of the virus in some form into the air, so that it has always been believed that the disease may be acquired by inhalation, like typhus. Scientific explanation of this method of receiving the virus is, however, still wanting.

Production of Epidemics. — While remaining fixed in one spot, plague varies very much in prevalence and intensity. When confined to sporadic cases, or existing only in the mild form, it is spoken of as endemic. When affecting larger numbers, and in a severer form, it is called epidemic. The disease is particularly liable to recur in periodical outbreaks; and in the countries affected popular belief has sometimes assigned a definite number of years, such as seven, for the interval. There is, however, no such regularity; sometimes a great epidemic is followed by several years of apparent immunity, sometimes the disease recurs several years in succession. The interval of apparent health is probably often filled, not so much with sporadic cases of severe plague, as with minor plague.

The causes of the development of minor into severe plague, and of the production of an epidemic, are very obscure. For various reasons it cannot depend upon the number of susceptible persons in the population;

the causes must be physical, affecting the biology of the plague bacillus whether in or out of the body. The best established fact is that epidemics have often (but not constantly) been preceded by a long drought. Epidemic diseases among animals, failure of crops, great abundance of lower forms of life — such as flies — and numerous other physical incidents, have been also described as preceding or accompanying plague, but are of little moment. More important are social conditions. Many epidemics of plague have followed on famines, wars, and other calamities, which produce destitution and lowered state of health. Other fevers have sometimes been observed to prevail at the same time.

Epidemics of plague always seem to terminate spontaneously, usually in from three to six months. Generally in each place they begin about the same season: this in northern countries is spring or early summer; and they are checked by the cold of winter. When prevalent in Egypt, plague used to begin in the autumn and end at the summer solstice, when hot south winds prevail. In Russia plague has on some occasions prevailed through the winter, being kept alive by the high internal temperature of houses. In Mesopotamia an air temperature of 86° F. at once checks an epidemic, and one of 113° absolutely stops it.

Conditions favouring the continued Existence of Plague. — It has been seen that no physical conditions, except temperature, have much effect on the prevalence of plague. But certain social conditions have a great influence, and seem almost indispensable to an endemic seat of the disease. The first of these is uncleanliness. All the localities in which plague flourishes are conspicuously filthy. The villages in Mesopotamia were in an incredible state of filth (Colvill). The sufferers from Indian plague were filthy beyond conception (Francis); the habits of the poorer classes of Chinese in Hong-Kong and Canton are notoriously of the same kind. A soil contaminated with fæcal discharges and decaying animal matter of all kinds appears to be an essential condition for the vitality of the virus. Among other causes of contamination must be placed cadaveric infection from bad customs of burial. This was notably observed in the Indian seats of plague, where the rocky nature of the soil offers obstacles to efficient burial; in Yunnan also, and formerly in Egypt. Dr. Creighton regards this as the dominant cause, but the general bearing of testimony hardly confirms his opinion. The burial among or within dwelling-houses of those who die of the plague has often, however, been a potent means of continuing the infection; such bodies contain bacilli in enormous numbers, and contagion from dead bodies is undoubtedly possible. Overcrowding of dwelling-houses (not necessarily correlative with density of population) and absence of ventilation are also powerful contributory causes. But of all social conditions poverty and general social misery seem to be the most influential. The poor are always the chief, sometimes almost the only sufferers, as shown by such epithets as *miseriæ morbus*, or "the poor's plague," often given to the disease.

But since destitution and uncleanliness are prevalent in so many

parts of the world where plague has never been heard of, these must be regarded as favouring, or perhaps essential, conditions for the disease, rather than as accounting for its origin. A very moderate improvement in sanitary matters at once limits or eradicates the disease.

Plague as a communicable Disease. — Unlike true miasmatic diseases — such as ague — there can be no doubt that plague is communicable, both from the sick to the healthy, and from an infected place to one previously uninfected; but the extent and nature of this communicability have been the subject of active controversy.

Communication from the sick to the healthy does not take place especially by contact, as was formerly believed (and hence the word contagion, with its false connotations, is better avoided), but by the atmosphere of the sick-room, or of the house itself; and this may be largely, if not completely, obviated by abundant ventilation. It may be difficult to say in some cases whether the infection is acquired from the patient or from the house; but it is pretty clear that communication from one person to another in the open air, or by casual meeting, is very rare, if it ever occurs. The transmission of infection by clothing, bedding, or other objects, that is, in the old phrase, by *fomites*, can hardly be questioned, though many exaggerated statements have been made on the subject.

Those who, like the French physicians in Egypt, denied contagion altogether, did so chiefly on the ground of their own personal immunity, though they attended thousands of patients, and performed many post-mortem examinations. One of them, Bulard, even wore the clothes of a patient who had died of plague, and Clot Bey tried in vain to inoculate himself with matter from a pestilent bubo. Many similar negative instances are on record; but much negative evidence is not so conclusive with regard to infection as a few positive cases. On the whole, the truth appears to be that during different epidemics and at different stages of an epidemic, plague differs immensely in its contagious property, as it does in its virulence; so that, broadly speaking, it is highly communicable at some times, and very slightly so, if at all, at others.

In explanation of cases where communication cannot be traced, it should be noted that, besides rats and the like, domestic animals may convey germs of disease, and Yersin has lately shown that the same is true of house flies.

Transmission of plague from one place to another not previously infected must also be regarded as well established; though, doubtless, this has often been wrongly assigned as the cause of purely local outbreaks. That this is possible by means of infected ships is clearly proved by the records of the Quarantine at Marseilles (quoted by Prus), when in several instances the infection was, so to speak, caught on the sieve — that is to say, the infected ships gave rise to cases of plague within the quarantine station, of which some were fatal. The like possibility on land has often been established, though doubted by the extreme school of anti-contagionists. For instance, in the London Plague of 1665, towns and

villages in communication with London became affected, though they were previously healthy, and had not suffered from plague for many years, if ever. The infection is doubtless generally conveyed by persons either affected with the disease or in the stage of incubation. Such persons convert the house they occupy into a focus of infection, till possibly the virus passes into the soil, and a severe epidemic may result. Conveyance by means of infected objects is doubtless possible, but probably much rarer.[1]

With regard, however, to this mode of transmission, it should be observed that, according to old and sound tradition, the plague does not spread when it is sporadic, but only when it is in an epidemic form. Furthermore, its diffusibility varies as much as its contagiosity in the narrower sense, being very marked in great epidemics, very slight or self-limited in others. Many epidemics have burnt themselves out on the spot, or travelled but a few miles; others have spread over whole continents. Generally successive epidemics, if unchecked, cover each time a somewhat wider area.

The rate of extension is also variable, but is generally slow. Plague has taken weeks or months to pass from one side of a city to another; it creeps along from point to point, so as to be compared by some to a drop of oil on paper.

Such gradual extension suggests the slow progress of a virus in the soil itself, and probably that is in some places the explanation; but, obviously, only transmission through short distances can be thus accounted for.

Transmission by the air cannot be said to be impossible, and was once much dreaded; but while this may be possible through distances measured by yards, it can hardly be so through distances measured by miles.

Plague as an Epidemic Communicable Disease. — *Clinical Forms of Plague.* — It is now pretty clearly established that plague may occur in two distinct forms, each of which may prevail separately to the exclusion of the other: — 1. *Pestis minor*, abortive or larval plague. 2. *Pestis major*, severe or ordinary plague. Very fatal cases of the latter are

[1] The instance of Eyam in Derbyshire (whither the infection was carried in a package from London) is well known; less well known is that of an isolated house (Oakhow) in Langdale, in which, as it is believed, every occupant died. A son of the house died of the plague in London in 1598 or 1665, and it is said that the infection was carried in his clothes, etc., which were sent home. Food was brought near the house by the neighbours, who, however, never entered it; the bodies were left where they fell, and it seems probable that the house was burned after the last death. A mound only remains, the site never having been occupied since. No cases occurred elsewhere in the immediate neighbourhood, but the pest fell heavily upon the towns of Cumberland and Westmoreland. Upon the wall of Penrith Church is the following inscription: "A.D. MDXCVIII. Ex gravi peste quæ regionibus hisce incubuit obierunt apud Penrith 2260, Kendal 2500, Richmond 2200, Carlisle 1196 Posteri, Avertite vos et Vivite, Ezek. 18th, 32." Vide *Lays and Legends of English Lake Country*, by J. Bagen White, F.R.C.S., Carlisle, 1873; and Dr. Barnes' paper in vol. xi. *Trans. Cumb. and Westd. Arch. and Antiq. Soc.* p. 158. In those days the fresh rushes were commonly laid upon those of previous years which were already charged and saturated with filth and refuse. — Ed.

sometimes called "fulminant," or *Pestis siderans;* but as they do not constitute an epidemic by themselves this is hardly a distinct form.

1. *Pestis minor* is characterised by the production of glandular swellings, with little fever and no severe general symptoms, lasting perhaps about fourteen days. It has been observed in Mesopotamia preceding severe epidemics of ordinary plague; in the city of Astrakhan in 1877 (the year before the severe outbreak in that province), and elsewhere. A similar type was observed in London in 1664, the year before the great plague, though its existence was concealed. This form is rarely or never fatal, and hence has often been overlooked or misunderstood. It does not appear to be contagious, and is not certainly known to be transmitted from one place to another. It has therefore the characters of an endemic miasmatic disease.

2. *Pestis major* may be developed out of the milder form. In endemic seats of plagues the mild form appears sometimes, probably from some change in the soil poison, to be rapidly transmuted into the severer form, which then appears as the epidemic form. Strange to say, gradations between the two forms do not seem to be generally observed, as the earliest cases of the true plague are usually the most severe. When the severe form is prevalent as an epidemic the disease is certainly transmissible. The extent and conditions of this transmission will be discussed later. The following clinical account is that of ordinary or severe plague: —

The Attack of Plague.[1] — *Incubation.* — The latent period between the reception of infection and the commencement of symptoms is imperfectly known, but appears to be generally from three to five days, or at most one week. Observation for about eight days may therefore be taken as sufficient to show whether a suspected person is or is not infected.

The symptoms of plague vary much in their intensity and relative frequency in different epidemics; but the order in which they present themselves and the general course of the attack are tolerably uniform.

Prodromal Stage. — Often the onset is quite sudden; but when preliminary symptoms (prior to the coming on of fever) are observed they are as follows: — The nervous system is chiefly affected. There is severe headache, vertigo, staggering gait, and appearance suggestive of drunkenness passing into lethargy. Colvill says — "The patient appears absent-minded, moves along speaking to no one, enters his house mechanically, shutting the door, and drops on to his bed, as if in despair or wandering in his mind." The pallid face, the injected eyes, the vacant or stupefied expression of countenance, with inability or refusal to answer questions, often suffice for an experienced eye to make the diagnosis. With these are associated the usual symptoms of acute febrile disease, pains in the limbs, extreme muscular weakness, and intense malaise. The tongue at

[1] In this summary I have followed chiefly the accounts given by Dr. Cabiadis and Mr. Colvill of plague in Irak. I have referred also to Dr. Cantlie's observations in Hong-Kong, and, for special symptoms, to those of other observers.

the beginning is thickly coated on the dorsum, the edges being red; later it becomes extremely dry and of a mahogany colour. Bilious vomiting or hæmatemesis are occasionally the initial symptoms. The prodromal stage, when present, may last a few hours or a day, rarely longer.

Febrile Stage. — Immediately after the above symptoms, concurrently with them, or sometimes from the beginning, high fever comes on, ushered in by a prolonged rigor or repeated shiverings. The temperature may rise rapidly to 102°, 104°, or even to 107° F. and higher. The pulse is always rapid, from 90 to 120 or 130. It is described as sometimes very small and thread-like, at other times not especially weak. Dr. Cantlie speaks of it as very variable in force, frequency and character. The skin is at first extremely dry, not always very hot to the touch. There is excessive thirst, with a sense of burning in the throat and stomach. Constipation is the rule during this stage. From the extreme weakness the decubitus is dorsal. The nervous disturbances are mainly those already described; sometimes they pass into active delirium, more often into lethargy and coma. The duration of the febrile stage would appear usually to be from two to five days, but sometimes it is much longer. The fall of temperature is generally described as sudden, and it may not rise again; but Dr. Cantlie observed in some cases a recurrence of high temperature after three or four days. In some fatal cases the rectal temperature after death was found to be high. In cases which do well there is a gradual but irregular fall, and after fourteen days the temperature is often subnormal.[1]

Buboes or inflammations of lymph-glands constitute the most important and characteristic feature of plague. They are rarely wanting, and then only in cases which are very rapidly fatal; though it is difficult to say in what proportion of cases they are absent, since in the panic of an epidemic they may be overlooked.[2] The term "bubonic plague" is therefore in the main accurate.

Buboes are in some instances the first symptoms to attract the attention of the patient, perhaps by a sudden lancinating pain. More usually they occur after the onset of fever, on the second, third, fourth, or even the fifth day of the disease. With the appearance of buboes there is often some abatement of the fever and general symptoms. The affected glands are generally extremely painful, but sometimes the enlargement is insidious, and only detected on examination. They may enlarge rapidly, more often gradually. Glands are usually affected in groups, but generally one is much larger than the rest. At first the glands are extremely hard, and in fatal or very severe crises may retain

[1] The temperature charts on pp. 930 and 931 are copied by permission from Dr. Cantlie's article, *Brit. Med. Journal*, 1894, vol. ii. p. 424.

[2] At Vetlanka in Russia, after the epidemic, I was informed by the relatives of those who had died of plague that there were no swellings, though there is reason to believe that such had occurred; the bodies were probably buried hastily in ordinary clothes and not carefully examined. In Mohammedan countries this would be less likely to happen in consequence of the ritual observances carried out after death.

this character to the last; in other cases suppuration occurs, which is regarded as a favourable sign, and is often more prevalent during the decline of an epidemic. On the other hand, rapid softening, flattening, or even disappearance of a bubo during the height of the attack is sometimes observed, and is a symptom of the worst omen, being speedily followed by death. It was so in London in 1665, and in recent

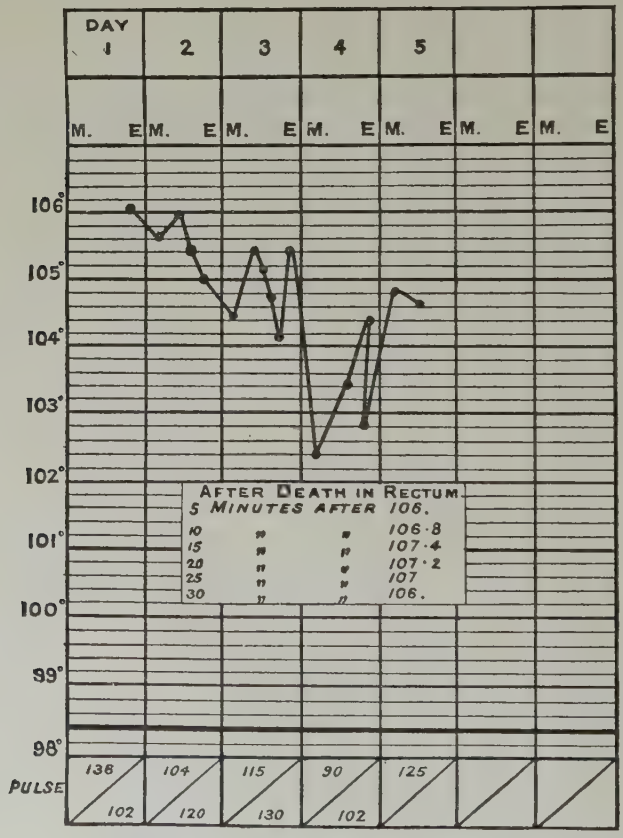

CHART 10. — Temperature chart of an acute case, with temperature in rectum after death.

epidemics in Irak. Sometimes the skin over the bubo becomes gangrenous, forming a carbuncle. According to Dr. Cantlie great œdema surrounds the glands, converting the group into an elevated doughy mass, sometimes five or six inches in diameter. A bubo once formed usually lasts during the whole of the attack. In suppurative cases which recover the process may be prolonged for several days, or even for some weeks, and leave formidable scars, the diagnostic marks of a past attack of plague.

The size of a bubo does not generally exceed that of an almond or a walnut, but may attain that of an egg or small orange. In the majority of cases (three-fourths or more according to some observers) only a single prominent swelling occurs: but Dr. Cantlie remarks that swollen glands are to be found in other regions if sought for. With regard to *situation* all observers agree that the inguinal group of glands is most frequently

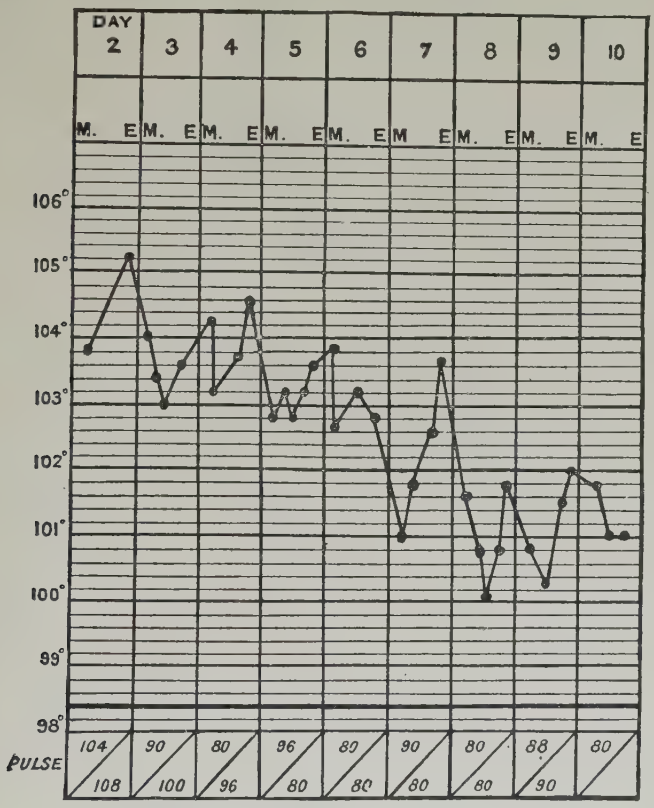

Chart 11. — Temperature chart of a less rapid case.

affected, such cases, according to Cabiadis and Colvill (if with these be included those of the femoral triangle), making 40–50 per cent of the total number; but where the femoral glands have been distinguished from the inguinal, the former appeared to be most frequently attacked. Next in frequency of attack come the axillary glands — in 25 or 30 per cent of cases, and in a larger proportion of female patients; the cervical and submaxillary or other glands are only attacked occasionally. Some internal glands, especially the various abdominal groups, are always found inflamed on post-mortem examination.

Of secreting glands the parotid is sometimes though rarely inflamed.

Carbuncles. — Gangrenous patches of skin, called carbuncles, though evidently not anatomically the same as the ordinary carbuncles proceeding from sebaceous glands, form another characteristic feature of plague. According to Cabiadis and Colvill, they occur, however, only in 2 or $2\frac{1}{2}$ per cent of the cases. Red patches appear on the skin, and become indurated and sometimes vesicular; then necrosis occurs, which spreads till the patch may attain a width of some inches. They may occur on any part of the surface of the body, and have sometimes been attributed to direct introduction of the virus of plague into the skin.

Petechiæ. — Purpuric patches, due to ecchymosis, sometimes of small size (petechiæ), sometimes larger, are often seen in severe cases. In the seventeenth century they were known as the "Tokens," and regarded as invariably indicating the approach of death.

General pustular or vesicular eruptions have rarely been observed.

Sweating is an extremely variable symptom. In certain epidemics very profuse sweats have been observed, in others this feature has been entirely wanting.

Hæmorrhage from various organs is sometimes observed in severe cases, and is much more frequent in some epidemics than in others. Epistaxis is a common form of it, but pulmonary hæmorrhage, usually associated with congestion or inflammation, is regarded as of specially serious import. It was observed in the first epidemic of the Black Death in Europe (1348), in the epidemic on the Volga in 1879, and on many other occasions. The theory of Hirsch, that this symptom distinguishes a special Indian variety of plague, comprising the Black Death of the fourteenth century and the Indian epidemics, is virtually abandoned by its author, and may be entirely discarded.

Hæmatemesis is sometimes so noticeable as to have been called "black vomit"; and intestinal hæmorrhage produces black dejections. Urinary hæmorrhage and metrorrhagia occur, and are generally or always fatal. The hæmorrhagic form of plague, though not constituting a distinct type, may be compared to the hæmorrhagic forms of small-pox, scarlet fever, and so forth.

The remaining symptoms will be best considered in relation to the various systems of the body.

Nervous System. — The general features have been already described. There is profound poisoning, affecting especially the cerebrum, but with little disturbance of motor functions, except occasional convulsions, and the contraction of tendons seen in the last stages of many febrile diseases. Paralysis does not appear in the descriptions. The violent or maniacal delirium of older records has not often been observed in recent epidemics.

Respiratory System. — The respiration is accelerated in the febrile state in proportion to the fever, perhaps more so. In some epidemics marked symptoms of engorgement of the lungs and pneumonia with profuse hæmoptysis are described, but no precise accounts of physical signs

are forthcoming. These cases have in some instances given occasion for the false diagnosis of an epidemic pneumonia. In Hong-Kong pulmonary symptoms were absent. These variations are probably connected with differences of climate and season.

Digestive System.— Beside the condition of the tongue already noticed, some cases give evidence of grave gastric disturbance, in the form of severe bilious vomiting; this is sometimes an early symptom, but it may occur at any stage. The bowels as a rule are constipated, but profuse diarrhœa sometimes occurs, and has been regarded (by Colvill and also by Cantlie) as a favourable symptom. The occurrence of gastro-intestinal hæmorrhage has already been noted.

Blood and Circulation. — No recent observations on the condition of the blood are recorded, but the French physicians in Egypt in 1835–36, a time when bleeding was customary, made some analyses, from which it appears that the blood coagulated imperfectly, and never formed a buffy coat. Its surface presented fatty globules, the serum was deeply coloured, and in some instances the reaction of free sulphuretted hydrogen was obtained. The water was in excess. These results are evidence of profound decomposition and destruction of red corpuscles. Recently in China the characteristic bacillus has been occasionally found in the blood, but never abundantly.

The *Circulatory* disturbances have been described.

The *Urinary System* presents nothing very notable. The urine is generally diminished, sometimes suppressed; but in the Hong-Kong epidemic it was normal. Hæmaturia has already been mentioned.

Duration of Attack. — Cases are sometimes fatal within a day, but in general the duration of fatal attacks is three to five days. Colvill, in Baghdad, found nearly one-fourth of his fatal cases died on the first day, about three-fifths within three days, and five-sixths within five; a very small number of such cases lived over a week. Hence if a patient lived as long as this, he was thought pretty certain to recover. On the other hand, cases in which suppuration of buboes occurs, and which recover, may be protracted to three weeks or a month.

Mortality. — Plague is the most fatal of all known epidemic diseases affecting large numbers. At the beginning of an epidemic the mortality is often 80 to 90 per cent or more of those attacked, and this rate is maintained or increased at the height of the epidemic. In the epidemic on the Volga in 1879, in one group of villages visited by myself, every person attacked by plague had died. Towards the end of every epidemic recoveries predominate over death, so that the average mortality falls: but in some limited epidemics in Irak three-fourths or more of those attacked have died. In the larger epidemics of Baghdad in 1876, the proportion of deaths was officially stated as 55·7 per cent; and at Hillah in the same country it was given by Cabiadis at 52·6 per cent. In other epidemics the percentage of fatal cases has not been more than 40 per cent, and in Egypt in 1834–35 about one-third.

The total mortality has notoriously been in many instances very

great both absolutely and in proportion to the population, though older accounts may have been exaggerated. The Black Death is calculated to have carried off one-third of the inhabitants of Europe, and in some countries more than one-half, but these estimates must be uncertain. In modern times it is said that the plague of 1830–31 killed 60,000 of the 150,000 inhabitants of Baghdad. The epidemic of 1876 in Irak is stated to have destroyed one-eighth of the whole population. In 1881 most of the villages affected lost a moiety or more of their inhabitants. As in such times a large part of the surviving population seeks safety in flight, it is easy to understand how villages may be entirely ruined and depopulated by the ravages of plague, as was the case also in our own country in the fourteenth century.

Prognosis. — The most unfavourable symptoms are hæmorrhage, in whatever form, and petechial eruptions or "tokens"; both affections are generally lethal prognostics. Profound affection of the nervous system is also an unfavourable sign. Suppuration of buboes is always of good omen. Sex and age appear to have little or no influence on the result. All observers agree that prognosis is generally very uncertain, and that cases apparently mild often terminate fatally.

Diagnosis. — No acute febrile disease presents the peculiar affection of the lymph-glands. Nevertheless a casual lymphatic inflammation or an inflamed parotid gland may occur in rare cases of other diseases, especially in typhus, which was at one time thought to show in some cases a transition to plague. Modern observers, however, have found no difficulty in making the diagnosis; the longer duration of typhus ("the fourteen days' fever") and the collective symptoms making a well-marked distinction. Malignant forms of malaria have sometimes been confounded with plague; but the absence of intermissions, or even of definite remission of the fever, and the inefficacy of quinine, are obvious distinctions. The aspect or facies of a malarious patient is also very different.

Morbid Anatomy. — There is little satisfactory information on this head; the fullest accounts are still those which were made up by the French physicians in Egypt in 1834–35; but some valuable observations were made also in the recent epidemic at Hong-Kong. The bodies of plague patients undergo rapid decomposition, and this change, especially affecting the blood, must have been the cause of some of the appearances described in older accounts, such as red or black staining of the serous membranes, of the surfaces of internal organs, of the mucous membranes, and so forth. The central nervous system, especially the brain, is deeply congested; the brain substance in some instances is softened, and the blood-vessels, especially the veins, much engorged. The lungs are much congested, especially in their posterior parts, but evidently this was partly due to hypostasis before or after death. The pericardium contains an excess of fluid, frequently blood stained. The right side of the heart is dilated with black, imperfectly coagulated blood, and the whole venous system is engorged. The heart substance is

pale, and sometimes softened. The stomach and small intestines may contain blood-stained fluid, sometimes actual blood, the surface showing intense venous congestion; but Dr. Cantlie, in Hong-Kong, found no congestion of these parts. In a few cases superficial ulcerations have been noted; but the Peyer's patches are not specially affected. The large intestine is comparatively normal. The peritoneum is described as showing great vascular congestion, chiefly venous. The liver was found enlarged by the French pathologists, sometimes considerably; but Dr. Cantlie found no notable enlargement: its substance is pale and anæmic, and presents the appearance of cloudy swelling. Hæmorrhage, interstitial or superficial, is found occasionally. The spleen, according to all observers, is greatly enlarged. The kidneys are sometimes enlarged, and occasionally present hæmorrhagic patches; Dr. Cantlie describes their histological appearance as being that of cloudy swelling.

The one characteristic sign is inflammation and swelling of the internal lymphatic glands, a condition always present even when the external glands are not notably enlarged. All groups of lymph-glands may be affected so as to form continuous chains, the cervical being united with the mediastinal and bronchial; the inguinal with the groups surrounding the iliac vessels and aorta, and with the pelvic glands, and so on. The mesenteric glands are least frequently affected. Agglomerated glands may form masses weighing as much as two pounds. In substance they are sometimes red, congested and hard, sometimes soft and discoloured, sometimes breaking down into a pulp. The surrounding tissue is infiltrated with serous fluid.

It is evident that, apart from the condition of the lymph-glands, there is nothing distinctive in the morbid anatomy of plague.

Treatment. — Nothing is less satisfactory than the treatment of plague. In old days opinions were divided as to the value of bleeding, but the balance of experience was decidedly against it. The violent sudorifics used in the seventeenth century appear to have been useless.

In modern times quinine has naturally been largely administered, but the general testimony is that it is quite useless. Antiseptics (such as carbolic acid, salicylic acid, etc.), antipyretics and cardiac stimulants have all been tried with no better results; purging with calomel and magnesia was largely used in Hong-Kong, but with little benefit. In fact, nothing approaching to a specific or antidote in the way of drugs has ever been discovered. The general principles of treatment would seem to be, as in other asthenic fevers, to give the patient an abundant supply of fresh air, to avoid overcrowding, to use cold affusions or baths in the height of the fever, and to administer such cooling or other drinks as may promote his comfort. When the strength is failing, stimulants are of course indicated, but alcoholic stimulation appears to be of less value than in typhus. In the seventeenth century some good observers denounced the use of "strong waters" as positively pernicious. In a malady of such short duration the utility of abundant nutrition would appear to be of less importance than in more protracted illnesses.

The local treatment of the buboes has received much attention. The general result of experience is that energetic treatment by caustics, mercurial inunction, or early surgical interference, is painful and fruitless. In early stages only soothing applications, such as poultices and anodynes, should be used. When softening or suppuration occurs, surgical treatment by incision and drainage is called for. There is no evidence of the value of thorough antiseptic surgical methods; but in the epidemic of Hong-Kong the injection into the glands of solutions of perchloride of mercury and carbolic acid seemed to be of temporary benefit.

Finally, it should be noted that Yersin, Calmette and Borel in the Institut Pasteur, claim to have worked out a system of *serum therapeutics for plague* like that used in diphtheria and other diseases. Repeated injections of virulent bacilli were made into a horse, and, after six weeks' preparation, its blood serum, when injected into rabbits, was found to be capable of producing, not only immunity against a subsequent virulent injection of plague bacilli, but also in larger dose the cure of animals previously submitted to a virulent injection.

Prophylaxis and Prevention. — For individual prophylaxis against contagion a number of elaborate precautions were formerly recommended, which need not now be taken into account. The important rules seem to be that any person, medical or other, who is brought into contact with infected patients or dwellings, should, in the first place, keep himself in as good a state of general health as possible; and, in the next, remain in the sick-room or house no longer than duty requires. The risk of touching and handling plague patients is apparently very slight, and nurses and attendants in well-managed and airy hospitals incur no special danger. Doctors on the whole have rarely been affected; and in most instances have conspicuously escaped. When they have suffered (as was grievously the case in the short epidemic of Vetlanka) it has generally been because they lived in the same dwellings, and under the same conditions as the affected population; or, as in Hong-Kong, they have been engaged in investigations on the material of the disease.

The prophylaxis of communities is a difficult matter, as it involves the question of quarantine, a system of regulations which has been elaborated chiefly to guard against this very disease; but the subject is too large to be fully discussed here.

Since there is no doubt that plague, when in an epidemic form, does tend to spread to other places and countries by means of infected persons or objects, we have to consider the possibility of its being brought to an uninfected place. The first precaution, and probably the best, consists in making the place unfit to be the nidus of the disease. This precaution concerns the purity of the soil itself, the cleanliness and ventilation of dwellings, the prevention of overcrowding, of extreme poverty, of personal uncleanliness and other insanitary conditions. It is improbable that any healthy European city or population in good sanitary condition could be the seat of a serious epidemic of plague. Since, however, sanitary perfection is not universal, and a very intense plague infection

seems sometimes to spread even under good sanitary conditions, the question of exclusion cannot be disregarded.

Total exclusion of persons and objects coming from an infected place, as common-sense shows, would be sufficient; but this is rarely practicable. The epidemic at Noja, in Italy, in 1815, was thus isolated by absolutely cutting off communication with other parts; and other instances might be quoted. But for general application, modified exclusion or "quarantine" is the only possible method. *Quarantine* consists in subjecting all persons and objects coming from an infected country to a period of observation measured by the known period of incubation of the disease, and in requiring certain measures of disinfection before they are permitted to proceed. In marine quarantine all ports in communication with an infected port, unless they adopt the same regulations, are themselves regarded as infected; arrivals from such ports are therefore put under the same restrictions — a serious matter for the commercial relations even of countries which do not adopt the principle of quarantine. In quarantine on land these arrangements are complicated with a so-called "cordon sanitaire" along the frontier to prevent entrance by irregular channels. In recent times infected districts have been surrounded by double or triple cordons to prevent exit except under quarantine regulations. These are necessarily military arrangements. On the efficacy of quarantine opinions have differed, though notwithstanding modern scepticism, it would be unreasonable to doubt that this system, as applied in former times in the Mediterranean ports, was of great service, especially as against infected ships. But early in this century the system became out of date, and even injurious through mal-administration. At the present time a modified system of quarantine against plague is still legally in force, and may be put in operation by an Order in Council; it is not, like other sanitary arrangements, subject to the Local Government Board.

The land quarantines established in Asiatic Turkey and Persia are considered by most unbiassed observers to be so defective as to be useless even if well designed. Some authorities, like Tholozan, deny their efficacy altogether, and regard the limitation of epidemics attributed to them as due to seasonal decline.[1]

Dismissing quarantine in the old sense, attention should be directed to ships arriving from an infected country with cases of plague on board, an element of the gravest danger which no sanitary authority could

[1] I can say from personal knowledge, that the limitations of the epidemic on the Volga in 1879 to a small district could not have been due to the elaborate cordons established by General Loris Melikoff, which in every newspaper were credited with the result. For two months the disease was confined to a single village, though communications on the main high road were open nearly the whole time. It then began to spread, but when the cordons were established it was already confined to a very few cases in another village. It is right to say that the villagers in their alarm established a sort of quarantine, or rather system of exclusion between one place and another. Much more credit is due to the radical measures of destruction carried out by the authorities. All infected houses (mostly of wood) and all suspected objects were burned: and it is highly probable that the disease was thus prevented from recurring in the next season or becoming endemic.

meet otherwise than by absolute isolation, followed by radical disinfection, or even destruction where practicable. The persons on board should be removed to an isolation hospital, and observed for a period corresponding to the known incubation of the disease. Supposing plague to be introduced into or to break out in any place, its restriction must depend upon the measures usually applied to infectious diseases, with special reference to the dwellings which may retain the virus. The infected house should be emptied, patients should be removed to a hospital, and the other inmates isolated under observation. Under some circumstances the patient might be better isolated in his own house, the chief thing to be avoided being concentration of the virus. The dwelling should in the meantime be thoroughly disinfected, and all clothing or infected objects subjected to disinfecting agents, of which heat appears the most efficacious. On account of its usually low degree of contagiosity, plague would probably in a clean city be more easily controlled than small-pox or typhus. As contagion from the dead body is possible, interment should be carried out under special precautions.

The only remaining question is whether the infection may be carried from an infected country to a distance by any kind of infected objects. As regards ordinary articles of merchandise, experience shows that the risk is slight or none; but the importation of rags or worn clothing might, as in the case of small-pox, be made subject to special restrictions.

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RELAPSING FEVER, OR FAMINE FEVER

Synonyms. — Five or seven days' fever; Five days' fever with relapses; Remittent fever; *Typhus recurrens; Fièvre à rechute;* Epidemic fever of Edinburgh, of Ireland; Epidemic remittent fever; Relapsing synocha; Bilious relapsing fever; Bilious typhoid; Remitting icteric fever; Famine fever; *Die Hungerpest;* Miliary fever; *Typhinia.*

This fever, with enteric or typhoid fever, formerly confused with the larger group of typhous continued fevers, was separated and distinguished by a long series of researches and of more accurate observations in the first half of the present century. The essential character which distinguishes it from typhus is the occurrence of the relapse; while from enteric fever it is distinguished by the absence of intestinal lesions. The following brief description has been given of it by Dr. Murchison: — "A contagious disease which is chiefly met with in the form of an epidemic during seasons of scarcity and famine. Its symptoms are: A very abrupt invasion marked by rigors or chilliness; quick, full, and often bounding pulse; white, moist tongue, sometimes becoming dry and brownish; tenderness at the epigastrium; vomiting and often jaundice; enlarged liver and spleen; constipation; skin very hot and dry; no characteristic eruption; high-coloured urine; severe headache, and pains in the back and limbs; restlessness and occasionally acute delirium; an abrupt cessation of all these symptoms, with free perspiration about the fifth or seventh day; after a complete apyretic interval (during which the patient may get up and walk about), an abrupt relapse on the fourteenth day from the first commencement, running a similar course to the first attack, and terminating on or about the third day of the relapse; sometimes a second or even a third relapse; mortality small, but occasionally death from sudden syncope, or from suppression of urine and coma; after death no specific lesion, but usually enlargement of liver and spleen." With this description before us it is easy to see how relapsing fever might be confused with typhus, especially if cases of it were few; as the relapse might be either overlooked or attributed to some accidental or unexplained conditions. But when cases became more numerous the points of difference would, as happens during epidemics, be forced into prominence, and the more so that during certain epidemics sometimes cases of typhus proper would predominate, and sometimes cases of the fever with relapse. When also it appeared, by and by, that patients who had been affected by the one form of fever contracted and went through a well-marked course of another, there could no longer be any doubt that two different kinds of fever were under observation. Dr. Henderson, of Edinburgh, was enabled in 1843 to advance arguments leading to the general acceptance of the view that relapsing fever must be distinguished as a separate disease from typhus fever. It appears now, in the light of further information, that relapsing fever is by no means a new disease. Dr. Spittal, of Edinburgh, stated in 1844 that Hippocrates described an

epidemic of relapsing fever as occurring under his own observation in the island of Thasos. The observations of Hippocrates are somewhat confused, some cases of doubtful character being described among many which may well have been instances of relapsing fever. Neither then nor now did cases run a perfectly definite course; but the accounts would lead us to believe that in most cases the disorder ran its course in seventeen days (*De Morbis vulgar*, lib. i.). Thus in two brothers who were attacked in the very same hour (the invasion having been therefore sudden), the phenomena were as follows: — In one the initial fever lasted seven days, in the other six; the intermission in one five days, in the other six; and the relapse in both five days, so that they recovered together (*De Morbis vulgar*, p. 956, see also pp. 953–956). In other cases the initial fever, intermission, and relapse lasted respectively five, seven, and five days; seven, seven, and three days; six, six, and five days; and again, six, seven, and four days. It will be seen that the addition of the three numbers in all these cases gives a total of seventeen days, which corresponds very well with the duration observed in modern epidemics. In Bradford, for example, during the course of the epidemic which I witnessed in 1869–70, the duration of the initial fever, intermission, and relapse respectively were seven, seven, and three days; eight, six, and five; five, eight, and four; five, eight, and five; six, seven, and four; six, eight, and three days, and so on. Out of sixteen successive and regular cases, omitting those in which a second relapse occurred, the whole duration of the disease was seventeen days in eight or one-half of the cases; in three cases the duration was eighteen days; in three, nineteen days; and in two, twenty days. Hippocrates dwelt on four important phenomena, whose occurrence at the period of crisis might be looked upon, separately or together, as of good prognostic omen. These were epistaxis, enuresis, diarrhœa, and dysentery. Sweating he also considered a favourable sign. That is to say, as we should put it, when secretion and excretion were free and abundant the cases did well; when otherwise, the reverse. The symptoms in his description are very characteristic. He mentions the splenic enlargement, the jaundice, the tendency of pregnant women to abort, as well as the frequent appearance of menstruation during the disorder. The first mention of the relapse is in these words: — "And about Arcturus" (the beginning of September) "many had the crisis on the eleventh day, and such had relapse without apparent cause." Some of the severe cases (many of which seem to have been fatal) appear, from the mention of the swellings, to have partaken of the character of plague. When suppuration occurred, such cases were always fatal.

It is a remarkable fact that, so far as I am aware, no reference to relapsing fever seems to be known between these highly interesting records of Hippocrates, and the time when Rutty wrote in 1770 describing the weather, seasons, and diseases in Dublin from 1725 to 1765. It seems incredible that relapsing fever was absent during the long centuries that elapsed between these two dates, yet no references to its occurrence appear to be extant.

Symptoms. — *The invasion* of relapsing fever is generally sudden. The patient is seized with rigors, headache, backache, and loss of strength; though the muscular weakness does not hinder patients from walking long distances to hospital, especially during the first day or two of the disease. In Bradford they would walk into the workhouse as late as the third or fourth day. I saw many cases, however, in which the symptoms appeared to set in gradually rather than suddenly. On the other hand, cases did occur very suddenly, like one I remember in a man, not himself a smoker, who was suddenly attacked while sitting among a number of smoking companions — the attack commencing with rigors, vomiting, and purging; but such suddenness as this was, so far as my recollection goes, comparatively rare. More commonly the patient had been ailing for some time before giving in to the attack, and would present himself with a white, moist tongue, and complaining of general malaise, rheumatic pains in the limbs and joints, and headache.

The invasion was not so gradual as to make it difficult to date the commencement, but it was rarely so sudden as, for instance, Dr. Murchison describes it to be — by no means so sudden as the onset of typhus or pneumonia. Still, on the whole, the writers who have recounted the symptoms seen in the various epidemics which have appeared in this country, especially those of 1819, 1826, 1828, and in the great epidemic of 1843, unite in the statement that the onset of the disease was sudden.

The period of incubation has varied in different epidemics. Sometimes the disease has broken out immediately after exposure to contagion; sometimes not till as many as fourteen days had elapsed. In Silesia in 1857 it was said to be longer — from a fortnight to three weeks.

But whether the attack come on suddenly, or be preceded by a period of anorexia or malaise, it is generally ushered in by rigors which may be slight or more severe, though they are generally severe. After being put to bed the patients complain of headache, generally referred to the occiput and vertex, and not, as a rule, accompanied by delirium. Pains are also complained of in the back and limbs. The skin is hot and burning, and the patient is restless with a flushed face, although the rest of the skin generally shows a characteristically yellow hue. The temperature, during the first few days of the attack, is high, ranging from 102° to 105° F. or even higher. The pulse also is quick, and is said sometimes to reach even 140 on the second day. In my cases it usually rose at that period to 110–120, and it appeared to me to be higher during the relapse — when it might rise to 130, or 140, or even 160 — than during the initial fever. These very high rates did not, however, seem to indicate any particular danger in the case. I saw very few deaths; but most of my patients were young adults, and, as will subsequently appear, they did not seem to have been much debilitated by hardship or starvation, and so were no doubt better fitted to struggle successfully with incidental illness. Although I did not observe any instance in which the pulse rose so high as 160 on the second or third day, I often saw a temperature of 104° F., and sometimes observed it as high as 105°.

Generally there was no rash, but in a considerable minority of my cases a rose coloured rash was observed, not unlike the spots of typhoid fever, but individually smaller. This rash was never petechial. It appeared on the thorax, abdomen, and limbs. In one case a rash was seen twice during the attack; the spot was from one to two lines in diameter, was rose coloured, and scarcely distinguishable from that of typhoid fever. All these rashes disappeared in a day or two. The second appearance of the rash occurred just before the defervescence at the end of the relapse.

Some interest attaches to the question of *rash* in relapsing fever. Dr. Murchison, who met with it in 8 out of about 600 cases, says it consisted of small spots, or of a reddish mottling: sometimes it resembled measles, but more often it was undistinguishable from that of typhus at an early stage; yet it always disappeared under pressure, and faded after a few hours, or within three or four days at the latest. It came out sometimes during the first attack, sometimes in the relapse, and either as early as the third day or immediately before the crisis. Petechiæ were not uncommonly present. It is suggested by Dr. Murchison that the rash in some cases was urticarial. What I saw, and not in one case only, but in many, was neither petechial nor urticarial. In the epidemic of relapsing fever in Silesia in 1857 a rose rash on the second or third day was the rule; and a considerable number of the cases seen in Bradford in 1869–70 showed the same feature, approximating, therefore, in character to those seen in Silesia rather than to those seen in other epidemics in this country.

The *respiration* is hurried, and varies from twenty-eight to forty a minute. A distressing cough is usually present, with rhonchus, sibilus, and harsh breathing on auscultation. I seldom saw expectoration, and in none of my cases did true pneumonia supervene; the symptoms indicated rather congestion of the tracheo-bronchial mucous membrane than congestion or inflammation of the lung itself.

These symptoms continue for several days, five to seven as a rule, but in some cases I have known them persist for as many as nine, the patient complaining most of the nausea and sickness, and of pains in the limbs and joints. The skin remains persistently yellow, and it is found in nearly all cases that the area of hepatic dulness is increased, while that of the splenic is always so. In some of my cases the area of splenic dulness seemed to be actually continuous with that of the heart, the spleen appearing almost as large as another liver. Patients then complained of weight and tenderness at the part. Tenderness was also well marked over the liver in many cases, corresponding with the occurrence of *jaundice*, which was present in nearly every case. As the latter was so common, occurring as well in slight as in severe cases, I cannot agree with those observers who look on it as a formidable symptom; but it is possible that different epidemics have shown widely different characters in this as in other respects. The jaundice has no necessary connection with head symptoms, and probably depends, as Dr. Murchison suggested, on functional interference by the fever

poison with the proper metamorphosis of the biliary products, which are retained in the blood instead of being eliminated by the liver.

The rest of the *digestive apparatus* also shows signs of disturbance. Generally speaking the tongue remains moist, and covered with a yellowish white fur. It is frequently red at the tip, and occasionally the whole organ may be seen brown and dry as in typhus. Frequent and persisting vomiting of greenish yellow matter is often observed. This symptom is in some cases most distressing, and may remain constant during the whole of the primary fever, disappearing during the intermission and reappearing during the relapse. Thirst is also a common symptom. The bowels are constipated as a rule, but in some cases diarrhœa occurs, and in others the bowels act every other day or so. *Pregnant women* almost always abort, but often not till the relapse occurs.

After these symptoms have continued for five, seven, or nine days, the severity pursuing an increasing or climacteric course, and the patient complaining much of the nausea and sickness, and of the pains in the limbs and joints, a *crisis* suddenly occurs. A copious perspiration appears, or diarrhœa or epistaxis, or two or more of these phenomena concur, often ushered in by a rigor (during which I have known the thermometer to register a temperature as high as 105° F.), and immediately the patient feels quite well. The temperature may then fall from 7° to 10° F., and the pulse from 136 to 70 or so; and the patient who, a few hours before, was tossing helplessly in the height of the fever, perhaps even with paralysis of the sphincters and pharynx, suddenly declares himself quite well, and is with difficulty prevented from getting up. The rheumatic pains, vomiting, headache, and all the febrile symptoms having disappeared, he will profess great surprise if he is told that there is another period of illness in store for him. The crisis occurred almost always during the night.

Although I might succeed in keeping my patients in bed for a few days, yet they generally got up towards the close of the interval, and before the *relapse*, which often therefore came upon them with all the force of the onset of a new disease. As, however, by no kind of treatment did it appear possible to prevent the occurrence of the relapse, and as therefore no hope could be held out that rest in bed might save the patient from its onset, it appeared the less desirable to interfere with the patient's own inclinations.

One of my patients had been out in India as a soldier, and had there suffered repeatedly from attacks of intermittent fever. He was quite certain that the illness from which he was suffering in 1870 was of the same character as the attacks with which he had been so familiar in India, and consequently felt quite incredulous when I told him he would have a relapse. After the manner of people of his class, he offered to lay a wager that I was mistaken, and that he would have no relapse. The relapse came, nevertheless, as predicted.

This incident is quite in keeping with what has been observed in

other epidemics, and reminds us of the classic case of Dr. Hughes Bennett, who had relapsing fever in the epidemic of 1843, when he was attended by Dr., afterwards Sir Robert Christison. When the patient was told by his medical attendant that "he was suffering from an attack of an old acquaintance" of Christison's, "whose face had not been seen for a good many years; that he had not yet done with it, and that he would have another attack, commencing with rigor, on the fourteenth day, Dr. Bennett expressed great astonishment." "Surprised," says Christison, "I will not say incredulous, Dr. Bennett replied that the relapse had no time to lose, as there were only two or three hours of the fourteenth day to run. It did, indeed, lose no time, for I must have scarcely reached home from his house before the rigor set in with violence."

The period of exemption from febrile symptoms — *the intermission* — is of variable duration. In my cases it usually seemed to last longer in those who defervesced early after the primary fever, and a shorter time when the primary fever had lasted longer. Thus the intermission extended to between nine and ten days in a case where the primary fever endured only six days; and only six days when the primary fever lasted between eight and nine. In the former case, therefore, the relapse took place on the fifteenth day, or between the fifteenth and sixteenth; in the latter between the fourteenth and fifteenth. But this rule is not invariable. The authorities state that the relapse generally occurs abruptly on the fourteenth day. It is ushered in by rigor. The duration of the relapse was from three to five days in the cases I saw. The usual duration appears to be three days.

A relapse occurred, so far as my observation extended, in every case without exception. The symptoms, similar to those of the primary fever, were often more severe; and one sometimes saw the tongue completely brown and dry as in typhus, and observed the pulse ranging at what, in other circumstances, would be considered the perilously high rate of 160. At the end of three or four days this set of symptoms usually came to a termination nearly, if not quite, as abrupt as that of the primary fever, the thermometer indicating a fall of 6° or 7° F., rarely of 10° F., and the pulse a corresponding diminution. The second crisis generally led to the establishment of complete convalescence, though sometimes a second relapse occurred. In such a case the symptoms were not so severe, nor the defervescence so sudden as before.

In none of the cases which I saw did a third, fourth, or fifth relapse occur.

It is worthy of remark that during convalescence, as well during the intermission as after the relapse, the temperature and pulse both invariably sank considerably below the normal standard, and gradually rose as convalescence became more completely established until the normal was again reached. This sequence is observed no doubt in most of the acute diseases, being in accordance with the general law of action and reaction; but it seems to me that the temperature ranges lower after the elevation of the febrile

stage of relapsing fever than in most other diseases. Thus a temperature of 96° F. was common at the commencement of the intermission; while in one of my cases, in which a second relapse occurred, the temperature during the second intermission was observed to be 94·5° F., 95·6°, and 96° on successive days. Even lower temperatures may be registered.

Two *temperature* charts are reproduced here. The first, that of R. D., æt. 30 years, is more or less typical of the records of temperature (and

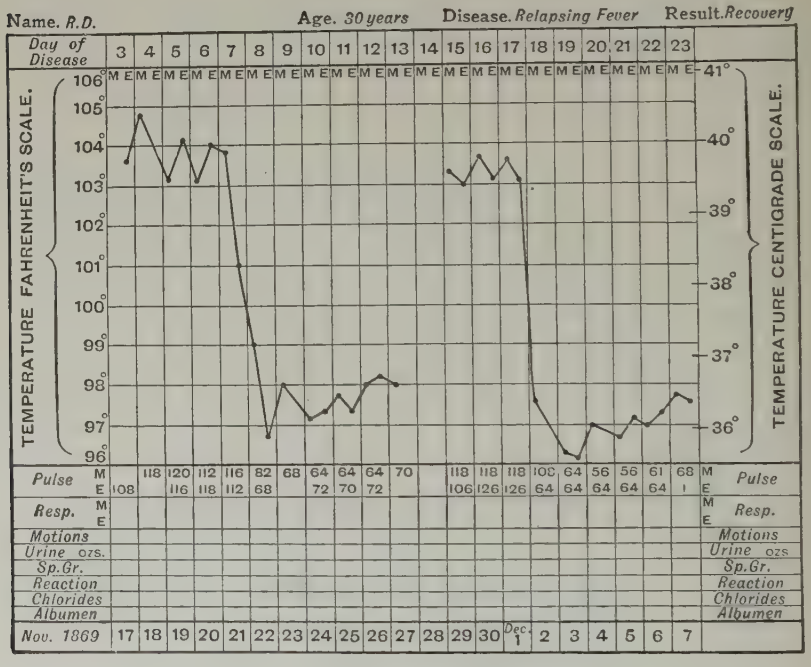

Chart 12. — Case of relapsing fever (Rabagliati).

pulse) found in relapsing fever. These ranges may be defined as two or more sets of high readings in temperature, alternating with periods of complete apyrexia. I have, unfortunately, no observations on the temperature at the very beginning of the fever (though I have one observation of 103·5° F. on the second day), but the authorities state that it is very high, agreeing in this respect with the early stage of typhus, but differing from that of typhoid fever. In the two charts depicted, the temperature was 103·5° F. on the third day in one, and 104° and 105° on the fourth day in the other. The second chart, that of J. O'H., is introduced to show the very great fall of temperature which is sometimes observed during the intermission. There is no fallacy in the observations which record temperatures so low as 95° F. and 92·2° F., for I took much

care to satisfy myself by repeated observations that these sublingual readings were correct. Between the highest and lowest recorded temperatures in the case of J. O'H. there is a difference of no less than 13° F., — a state of things which, if not unique in medical thermometry, is at any rate extremely rare. Chart No. 1 (and indeed No. 2 also, except that the fall in the intermission is greater than usual) shows so well the

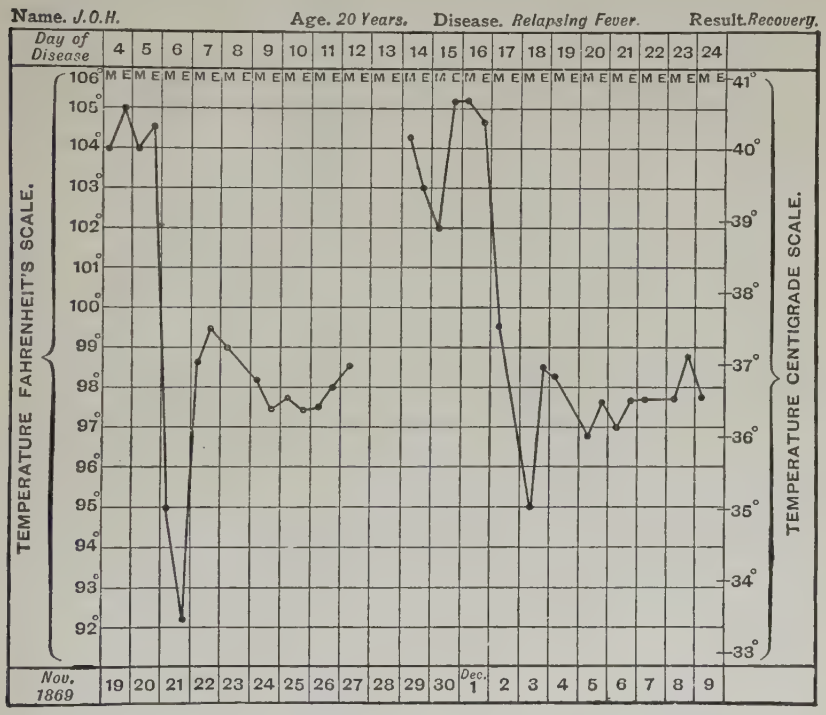
Name. J.O.H.
Age. 20 Years.
Disease. Relapsing Fever.
Result. Recovery.
Day of Disease
4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E
106° 105° 104° 103° 102° 101° 100° 99° 98° 97° 96° 95° 94° 93° 92°
41° 40° 39° 38° 37° 36° 35° 34° 33°
TEMPERATURE FAHRENHEIT'S SCALE.
TEMPERATURE CENTIGRADE SCALE.
Nov. 1869
19 20 21 22 23 24 25 26 27 28 29 30 Dec. 1 2 3 4 5 6 7 8 9

CHART 13. — Case of relapsing fever (Rabagliati).

course of the temperature in relapsing fever, that the reader may be spared a verbal description.

The *pulse rate* is also characteristic of the cases seen in the Bradford epidemic. The usual accounts, however, state the pulse rate as higher than is shown in the chart. Thus 140 is said to be not uncommon, while 160 is said to be occasionally reached. An interesting point is that, as I have said, these rates do not seem to imply danger to the patient, much less do they prove the forerunners of a fatal termination. As with the temperature, so with the pulse, a sudden and extensive fall occurs at the end of the primary attack, and also at the termination of the relapse. One of my observations records a fall from 148 to 80, or of no fewer than 68 beats a minute in the course of a few hours. A fall

from 120 to 60 in a night was quite a common occurrence. Like the temperature, the pulse also usually falls below normal before returning to its natural rate. Thus it remained for about a week at 60 a minute in a young fellow of eighteen, whose normal pulse rate was much higher than that. The pulse and temperature, as might be anticipated, usually rise and fall together, though this is not always the case. Sometimes the rise of one precedes that of the other, and may be symptomatic of the general fever about to supervene. Both temperature and pulse gradually reach normal as convalescence becomes established.

The only fatal case which occurred in my practice was of an old woman of seventy. She died, like one of Hippocrates' cases, on the sixth day. As she did not live long enough to have the relapse, there was just that amount of doubt as to the diagnosis which must attach to every such case; but I had no doubt that the malady was relapsing fever.

This course of the general symptomatology of relapsing fever is then very characteristic, and no one looking at these temperature charts could possibly mistake them, or confuse them with those of any other disease. No doubt anomalous cases occur. This is so in all epidemics, and not of relapsing fever only. In one case of mine the disease ran on for thirty-six days, and seemed to be a case in which typhoid and relapsing fevers were mixed together; although perhaps other explanations of it were possible. Yet the characters of the disease, as it was generally met with, were so striking and peculiar as to be readily separable from those of any other disease, and to leave no doubt on the mind of the observer as to their true character.

Etiology. — *Remoter Causes.* — So far as I saw, the male sex was much more liable to relapsing fever than the female. Dr. Murchison gives the proportion as 116 to 104, but inclines to the opinion that sex has very little influence in the matter. If the male sex suffer more than the female, it is probably because men are more exposed to the exciting causes of the disease. As to age, relapsing fever (like other fevers) is especially a disease of early life. Most of my cases occurred in young male adults. Dr. Murchison gives the mean age as 24·4 years. As to occupation, almost all the cases were either among paupers or very poor persons. This has been the general rule in epidemics of the disease, a fact which is so notorious as to have given a name to the disease. At the same time, it must be said that careful inquiry in Bradford often failed to elicit the fact that the sick had had to undergo any special hardships, or to endure any special privations in food. Trade was then moderately good in the town, and the consequent demand for labour was pretty active. In Liverpool at the time of the epidemic of 1870, according to the *Lancet* report, "there was full employment for every able-bodied and industrious man." The patients themselves did not show any signs of having been deprived of food. Of 522 patients of whom the inquiry was made, only 91 had been in the workhouse before, which shows at least that they did not belong to the habitual pauper class. Besides this, at the time of the

Liverpool epidemic, there were (1st) considerably fewer inmates resident in the workhouse, (2) considerably fewer families in receipt of outdoor relief; (3) considerably fewer patients suffering from zymotic diseases than in the corresponding period of the year preceding. From all these circumstances it appears as if the name of "famine fever" is not always an appropriate one. Other circumstances appear to enter into the causation of the disease. Mere overcrowding is not a sufficient cause, as some very overcrowded populations have suffered even less from it than others less densely packed. The *Lancet* report on the Liverpool epidemic in 1870 showed that there were at least three principal causes, namely, (*a*) the sites of the houses, which were frequently placed on decaying vegetable and animal matter and midden refuse; (*b*) insufficient and imperfect drainage; and (*c*) the extensive prevalency of cellar dwellings in darkened and filthy courts.

On the other hand, much evidence exists to show that there is as a rule some connection between the occurrence of relapsing fever and the existence of destitution among the population attacked. Contagion cannot explain the whole of the cases or the spread of epidemics. Not to mention the fact that in Bradford and Liverpool in 1869–70 the mass of the cases of the disease occurred among the pauper class, Dr. Murchison showed that in London 97·5 per cent of the cases investigated by himself were paid for by the parochial authorities, and were totally destitute. Nine of the remaining cases (430 in all were investigated) were admitted free, and were also destitute. Not a single patient had been a servant in a private family, and in one instance only was a fee for admission paid by the patient's friends. It is probably, also, not without significance that the epidemics of 1817, 1818, and 1819 raged during a period notorious in British history for low wages, high prices of food, and general depression due to the fall of the inflation of the markets caused by the great continental war; while the epidemics of 1843–4 and of 1847–8 occurred about the time of the great Irish famine, and during the general destitution which played so great a part in causing the abolition of the corn laws, and in preventing their re-enactment. In 1826 Stokes described relapsing fever as famine fever, and in 1847 Corrigan's pamphlet bore the title, *On Famine and Fever, as Cause and Effect in Ireland.* When the epidemic occurred in Silesia, in 1847, the inhabitants, in consequence of a succession of bad harvests, had been reduced to subsist on clover, grass, mushrooms, and the roots of trees. The synonym "Hungerpest" points unmistakably to the connection, in German opinion, between relapsing fever and the existence of destitution. "Carter states that it was brought to Bombay in 1877 by the peasantry flocking into the city from famine-stricken districts" (Fagge). Dr. Murchison's view, as is well known, was that relapsing fever is due to destitution, while typhus is produced, he thought, by overcrowding and destitution combined.

Immediate Causes — Contagion. — The question of the contagiousness of relapsing fever was very fully gone into by Dr. Murchison, who proved his position that it was an exceedingly contagious disorder in the same

way that he did for typhus fever. Several facts in corroboration of his opinion came under my notice. Thus several cases were admitted to hospital from the same house or street under circumstances which left little or no doubt that some patients had been infected by others. In one case, again, early in the epidemic, and before I was accustomed to recognise and diagnose the fever, I ordered a patient suffering from it into the general ward, thinking he had rheumatism. It was not long before I had to order the removal both of him and of another patient, who lay beside him, to the fever hospital. Both had relapsing fever, and the other patient had been some time in the general ward. However, no nurses or attendants on the sick in Bradford took the disease from patients. I suppose this good fortune was due to the fact that our cases were not very numerous, and perhaps also to the further fact, that our fever hospital was roomy and airy, rather than that our cases were not so infectious as they have been in other epidemics. At any rate both in 1818 and in 1843 relapsing fever appeared as a very infectious disorder. Thus Dr. Welsh says of the epidemic of 1818, that in the course of four months his three colleagues, two of the young men in the apothecary's shop, two housemaids, and thirteen or fourteen nurses, caught the disease; and the matron and one of the dressers died of it. In Queensberry House in 1818 two medical men, the matron, two apothecaries in succession, the shop boy, washerwoman, and thirty-eight nurses were infected, and four of the nurses died. Of the epidemic of 1843–4 Dr. Wardell wrote: "Most of the medical officers connected with the Edinburgh Royal Infirmary, and additional fever hospital, were seized with it: eight of the resident and clinical clerks in quick succession became affected." . . . "The majority of the nurses and domestics took the disease, and of the former, at one time, no less than nineteen were labouring under it." And more to the like effect. The late Dr. Begbie, from his experience of the epidemic of 1847, arrived at the conclusion that relapsing fever, like typhus, was communicable from "the sick to the healthy; that for this purpose actual contact with the sick was not necessary, the subtle poison of this form of continued fever, equally with that of typhus, being readily conveyed through the air surrounding the latter; and, lastly, that by means of fomites or clothes the disease may readily be propagated."

A. R.

Bacteriology. — Although Henderson of Edinburgh, in 1843, had distinguished relapsing fever from other diseases with which it had been classed under the general term "typhus," it was not until 1873 that Obermeier, assistant to Professor Virchow in Berlin, demonstrated the presence of lively spirilla in the blood of patients suffering from the disease. This observation has been generally corroborated by later observers.

The micro-organism of relapsing fever is a long and slender spirillum, of varying length (16 to 40 μ), sinuous, or twisted spirally in 10–20 turns. In fresh blood the spirillum is seen to be flexible and very active. Its movements are progressive, with undulations passing wave-like along

from one extremity to the other. It is so fine that under a low power its presence is revealed only by the commotion among the blood corpuscles, which by the rapid movements of the spirilla are thrust violently aside. The spirilla are much thinner than a cholera vibrio, and their ends are tapering and sharp. These thin tapering ends were formerly considered by some to take the place of flagella, but Koch has since demonstrated true flagella, which account for their rapid motion. The rapidity and intensity of the movements depend, according to Dr. Vandyke Carter, directly on the number of the spirilla.

Activity persists after the death of the diseased person, and can be studied for a long time in preparations in one-half per cent salt solution, or in blood serum.

Heydenreich found that the vitality of the spirilla, as evidenced by mobility, could be preserved for a time varying from two and a half hours to fourteen days, according to the temperature at which they were kept; at a higher temperature the movements ceased sooner.

The presence of the spirilla in the blood has been taken as evidence of their aerobic nature.

Although it has been found impossible to cultivate the bacteria of relapsing fever in or on artificial media, Koch has observed the formation of tangled masses, and an increase in the length of spirilla which had been placed in tubes of blood serum.

The total disappearance of the spirilla from the blood after the pyrexial attack, together with their reappearance in the next paroxysm, led some bacteriologists to the probably erroneous conclusion that they produce spores, in which form they were assumed to remain dormant until the next relapse.

Metschnikoff has shown, however, that, after the parasites have disappeared from the blood, masses of them may still be present in the spleen, where they are mostly enclosed in cells. Many of these cells seem to be undergoing degeneration, and it is possible that the contained bacilli may then escape in a condition capable of causing the relapse. On the other hand, those microbes which had not been engulfed, and had remained extracellular, may be responsible for the second febrile attack.

The low temperature by which the infective nature of the blood of a patient is destroyed seems to point to the absence of spores, although Soudakewitch has described spirilla which showed distinct terminal swellings. Free globular bodies are also observed, which, from their size and appearance, may be these swellings detached from the spirilla. Carter had some years previously called attention to the irregular dotted, beaded, or clubbed appearance chiefly to be observed in dried specimens. From the spirillar nature of the organism it is highly improbable that it forms ordinary endospores; it is more likely that reproduction takes place by fission, the spirillum dividing into two equal parts.

The organism stains readily with the ordinary basic aniline dyes, such as gentian violet, bismarck brown, and fuchsin.

The spirilla are to be found in the blood for some hours, or even one or two days before the crisis, but after the crisis they generally disappear quickly.

The micro-organisms persist throughout a pseudo-crisis, and are not to be found in the non-febrile intervals between the true attacks.

At the beginning of the pyrexia the spirilla are seen to increase in number until at the crisis, according to Carter, they may be in the proportion of one-twentieth to one-tenth the total number of red blood cells. There is then a diminution, until in a short time none is to be observed in the blood.

The constant occurrence of this micro-organism in all of Obermeier's cases, and its invariable absence in other diseases similarly examined, point to its causative relation to the symptoms. That it has been found impossible to cultivate the spirilla in artificial media can hardly be considered a serious objection when we consider the following facts: —

Carter, working in India in 1879, while verifying the observation already made in Europe, gave the following as reasons for connecting the presence of the spirilla with the fever symptoms in the disease: —

1. The blood infection is always followed by the characteristic fever, although an interval of some hours or even one or two days may intervene.
2. With the advent and progress of pyrexia the spirilla increase in number, but there is no fixed relation between the type and intensity of the fever and the number of organisms present in the blood.
3. They disappear with the cessation of fever, persisting, however, occasionally for a day or two, especially during pseudo-crises and slow defervescence.
4. By inoculation of defibrinated blood removed during the period of pyrexia — and therefore containing the spirillar organisms — from a patient suffering from relapsing fever into a healthy person, the disease may be conveyed to new subjects.

The disappearance of the spirilla from the blood in man during the apyrexial periods is as yet unexplained; though Metschnikoff's observations have been taken as evidence that they are largely, if not altogether, destroyed by the phagocytes, which engulf them and carry them to the spleen. This organ is enlarged, and is the seat of the chief pathological changes in those cases in which death from the disease occurs; it is then seen to be filled with white cells containing the parasites. The liver and marrow of the bones contain foci of necrosis.

Koch, Carter, Metschnikoff, and Soudakewitch, by inoculation experiments on monkeys, have produced symptoms which correspond to the disease in man; by this means they have thrown much valuable light on the pathology and bacteriology of the disease, and have established its specific nature. In these animals inoculation was followed by a sharp febrile attack, beginning usually in about three days. The disease ter-

minated, without relapse in recovery. Spirilla were observed during the pyrexia, but disappeared soon after the temperature had fallen; and in animals which had been killed ten hours after the crisis the parasites were found only in the form of débris, chiefly contained in the microphage cells in the spleen.

An emulsion of spleen-pulp, containing the spirilla, produces, when injected into a second monkey, the same symptoms and fever. A monkey that had passed through an attack remained susceptible to a second inoculation; recovery is not followed by immunity.

Although under ordinary conditions the monkeys invariably survived, Soudakewitch showed that on removal of the spleen the disease proved fatal to some of the monkeys. The temperature gradually subsided until death occurred. On examining such animals after death the blood was found to be swarming with spirilla; in one instance the inferior vena cava was nearly blocked by tangled skeinlike masses of these organisms.

F. F. Wesbrook.

Relation between Relapsing and Typhus Fevers. — Some interest attaches to this subject. We have seen that Dr. Murchison thought that, in the matter of causation, there was some relation between these two diseases; he believed that relapsing fever was caused by destitution, while typhus fever was due to destitution and overcrowding. In the matter of the bacteriology of the two diseases no such relationship appears to have been as yet determined. While the bacteriological cause of relapsing fever seems to have been made out, that of typhus fever has not. If ever the latter is discovered, it will be interesting to notice whether in genus or species it is related to the former. At any rate as regards the progress of the two disorders in different epidemics a well-marked relationship has been seen. The sequence has generally been that in epidemics of relapsing fever well-marked cases have been most numerous in the commencement of the epidemic, while cases of typhus were comparatively rare. As the epidemic advanced the cases of relapsing fever have become comparatively fewer, while those of typhus have become comparatively more numerous. Towards the close of the epidemic, on the other hand, the cases of typhus have become much the more numerous, while those of relapsing fever have been comparatively rare. Even as early as 1826 the distinction between the two fevers had been observed, but in 1843 it was more particularly insisted on, especially by Dr. Henderson. In Glasgow Infirmary, for instance, there were admitted 2871 cases of relapsing fever in 1843, and only 142 of typhus. In 1844, 432 cases of relapsing fever were admitted, and 711 of typhus; while in 1845, only 37 cases of relapsing fever were received, and 266 cases of typhus, the mortality being, as might have been expected, much higher in the typhus than in the relapsing fever cases. In 1869–70 I saw a good many patients who first contracted relapsing fever, and in the course of a few weeks there-

after took typhus. I did not see any who took typhus first and had relapsing fever afterwards; and I doubt if there were any patients in Bradford in whom this sequence was observed. Such a sequence may, of course, have occurred in other epidemics.

In those cases in which typhus fever followed relapsing fever in the same patient within a short interval of time, it seemed to me that the typhus pursued a milder course than it might have been expected to do had the patient suffered primarily from typhus. This is not altogether what might have been anticipated. We might rather have anticipated that the patient, debilitated by the previous occurrence of relapsing fever, would thus have been brought into greater danger on the subsequent occurrence of typhus. My observations were not perhaps numerous enough to allow me to generalise from them; but I confess that, such as they were, they did raise the question in my mind whether the two fevers might not have some causal relationship. May not the causes of relapsing fever and typhus fever be so closely connected, that the occurrence of one of them in a patient may modify the subsequent course of the other? In vaccination and small-pox, for example, we have such a sequence of events, and without laying too much stress on it, it seemed to me that the facts of the Bradford epidemic might justify some such reflections.

Be this as it may, a relationship between the numbers of cases of relapsing and typhus fevers has been observed as a rule in epidemics since the time when the two fevers were first distinguished. And even before this time an investigation into the mortality at the beginning, middle, and end of epidemics has rendered it almost certain that a similar incidence of cases of relapsing fever and of typhus fever has occurred.

During the continuance of the visitation of epidemic diseases the mortality, as a rule, is highest at the onset of the epidemic, diminishing gradually as the epidemic advances. This may be because the most susceptible are first attacked, and take the disease in its most virulent form. "Increase of susceptibility" may be mistaken for "increased virulence" of disease, the former expression referring rather to the nature of the soil, so to speak, in which the disease finds a lodgment; while the latter refers rather to the nature of the seed than to the characters of the soil. Another reason for the diminishing mortality observed as epidemics advance in time may simply be that the disease assumes a milder form which we are unable to account for. In epidemics of relapsing fever, on the other hand, even before it was properly distinguished from typhus fever, we find records of a low mortality at the beginning of the epidemic, of an increasing mortality as the epidemic advanced, and of a mortality which was highest towards the close of the epidemic. This was particularly noticed in the epidemics of 1817–18, and in 1819; the most probable inference seems, therefore, to be that there was a mixture of cases of relapsing and of typhus fever, and that their relative frequency at different periods of the epidemic determined the observed mortality.

If that were so, as it appears to have been in 1817–19, as it certainly was in 1826–28, when the distinction between relapsing and typhus fevers was first made, and in 1843 and onwards, when it was generally accepted by the profession through the labours mainly of Dr. Henderson, it seems reasonable to suppose that, as a rule, relapsing fever and typhus fever have at other times borne to one another the relationship which has been shown to exist in those epidemics.

Diagnosis. — The relationship already dealt with is to some extent helpful in the diagnosis of relapsing fever. As a rule, the severity of the onset is greater than in typhoid fever, and the absence of abdominal symptoms serves still further to distinguish it; although, of course, in some cases of typhoid, abdominal symptoms may be in abeyance, and on the other hand, in a few cases of typhoid the onset of symptoms may be both sudden and severe. As the cases progress the differences become more marked. Before the eruption of typhoid fever is due, a sudden defervescence will have revealed that the attack is one of relapsing fever. From typhus, again, the absence of rash in the majority of the cases of relapsing fever (though we have seen that in some cases a less characteristic rash has appeared both in this country and abroad) will serve to distinguish it. In both typhus and relapsing fever the onset may, of course, be sudden. But as between typhus and relapsing fevers the great and obvious difference is the sudden defervescence that characterises the latter at about the end of the first week; and this short convalescence will also serve to distinguish relapsing fever from pneumonia, in which the onset is likewise often sudden.

From small-pox the diagnosis is comparatively easy after the third or fourth day, the shotty eruption under the skin of the wrists and on the face in variola being never present in relapsing fever. In influenza — the epidemic which played such havoc with our people in 1891, and which has reappeared to greater or less extent every year since — the symptoms are as sudden as in relapsing fever; but they persist for a shorter time in mild cases, while in severe cases of influenza, broncho-pneumonia almost always occurs. In influenza there is no sudden recovery and no subsequent relapse, the symptoms in influenza progressing pretty steadily to death or to some degree of convalescence.

All these points of difference which serve to distinguish relapsing fever from other diseases, such as typhoid and typhus fevers, small-pox, and pneumonia, are open to the objection that time is necessary for their appreciation. Is there no character, it may be asked, which will enable us at an earlier period to say positively — this is or is not relapsing fever? The demonstration of the microbe proper to the disease would do this; and Dr. Carter, of Bombay, says that no less than 25 per cent of his cases were irregular. In 1869 I was not aware of the existence of the microbe of relapsing fever, so that I was not able to use it for diagnostic purposes. If, however, a new epidemic were to attack us, I think it would be found that the chief means of diagnosis would be time, as it has been in previous epidemics; especially as an observer might or might not think of relapsing

fever if he had not had to treat it before. The discovery of the *spirochæta* would make the diagnosis sure.

Sequelæ. — These are not common in relapsing fever; with the termination of the attack itself the patient nearly always recovers, unless the illness occur in a very debilitated subject. In such persons as these the consequences, chiefly pulmonary, with which we are familiar in other fevers, may follow relapsing fever. *Parotitis* must be especially mentioned, not because of its frequency in Great Britain, where on the contrary it is very rare, but because in some epidemics — as in that which occurred in Russia about twenty-five years ago — its comparative frequency has led to the rumour of plague. Parotitis is occasionally seen in typhus, and enteric fever likewise.

Prognosis is greatly determined by diagnosis. In relapsing fever we know that the mortality is not more than 5 per cent, while in typhus it may approach 20. The cautious physician will judge of each case on its merits, and after he has diagnosed relapsing fever, as he will no doubt be on the lookout for cases of typhus fever in the later phases of the epidemic, he will remember that a much higher mortality may then be looked for, although of course it will still remain true that relapsing fever has a low mortality. The higher mortality will probably be due to intercurrent typhus fever, and not to relapsing.

Morbid Anatomy. — Although the cases which I saw exhibited a very small mortality, and although, therefore, my opportunities for inquiry into the morbid anatomy of relapsing fever were almost nil, it has not been so in all epidemics. In Berlin, for instance, in 1872–73, not fewer than 100 fatal cases occurred in the Charité Hospital alone; and there were therefore numerous opportunities of making careful inquiry into the morbid anatomy. The organs in which the most marked changes were found were the spleen and blood, the liver, the heart, the kidneys, the bones, and the muscular tissues. The most important changes of all, both as regards structure and gravity of import to life, were those found in the spleen and heart.

An alteration was commonly observed in the muscular tissue of *the heart*, so grave as frequently to account for the fatal issue. The organ was flabby, the muscular tissue throughout pale, of a dirty gray-yellow colour, and friable. The primitive muscular fibrils were in many cases found to be fatty. The fattiness and general degeneration found in the heart in relapsing fever equalled that seen in the most malignant septicæmic and puerperal fevers, and in diphtheria.

The spleen was very much enlarged, and at the same time softened and fatty. In different observations it is described as weighing (as compared with its normal 4 ozs.) in one case as much as $4\frac{1}{2}$ lbs. avoirdupois, in another over 2 lbs. (920 grammes), in another about $1\frac{1}{2}$ lb. (670 grammes), in another 15 ozs., and again about $\frac{3}{4}$ lb. (330 grammes). The enlargement of the organ was greater than occurs in any other affection except leukæmia, and consisted of two sets of changes, a diffuse general enlargement, usually accompanied with noticeable softening, on the

one hand; and on the other the appearance of small yellow softened patches which in some cases reached the size of a horse bean. Some observers have believed these patches to be due to infarctions. The enlargement took place in all directions, the capsule being tightly stretched and shiny, the tissue substance softer than usual, though not exactly diffluent; the spleen-pulp dark blue-red, standing out strongly; the follicles considerably enlarged and often obliterated; their colour for the most part gray, though sometimes pure white or yellowish. The swelling of the spleen-pulp was mainly due to marked congestion of the vessels, and an abundant increase of the cell elements.

As regards the morbid anatomy of the *liver*, some difficulty occurred in distinguishing the recent effects caused by relapsing fever from those frequently pre-existing effects caused by alcoholism in the same patients. But, so far as could be made out, the increase in the size of the liver was greater than has been observed in any other of the infectious diseases. In one case the liver weighed 3620 grammes — almost 8 lbs. avoirdupois — an enormous increase. The organ was enlarged throughout, the lobules being also increased in size, so that their boundaries were rendered obscure; the cut surfaces were cloudy, and of a striking uniform gray-red colour. On microscopic examination there was found cloudy swelling of the hepatic cells with fatty infiltration round their edges, and fine-celled infiltration along the portal vein. Jaundice did not seem to bear any relation to the gravity of the cases, being well marked in some slight cases. On the other hand, out of sixty-five fatal cases only sixteen showed the presence of this symptom.

The *kidneys*, like the liver, were also much increased in size, sometimes weighing even twice their normal weight. The parenchyma was found soft and flabby, the cortical substance widened and filled with cloudy swelling, the vessels and the Malpighian corpuscles for the most part pale. In other cases the cloudy swelling was found for the most part in the straight tubules. There were found, besides, more or less abundant dark red spots specially numerous near the surface; and, converging thence in a radiating manner towards the papillæ, they could be traced, as red or brown spots or stripes, deeply into the tissue of the pyramidal substance. On microscopic examination it was found that not only were the tubuli more or less fatty, but also that the lumen of the urinary tubuli was filled partly with transparent fibrinous material, and partly with hæmorrhagic clots in the most diverse stages of coloration. For the most part these were met with in the under parts of the tubuli contorti and of the loops of Henle; the hæmorrhages were often found also between the capsule of Bowman and the interlacings of the vessels of the glomeruli. And as, besides these conditions, an abundant infiltration of small cells was found in the interstitial tissue, all the anatomical conditions were evidently present for the subsequent onset of Bright's disease.

In the *lungs* were found marks of hepatisation and pneumonic

infiltration; also in some cases bronchiectasis and bronchitis. In others old apical cheesy and chalky deposits were found which might or might not have been caused by the disease.

The condition of the *blood* of patients suffering from relapsing fever was related to the organism found to be present in the disease, and has been dealt with under the bacteriology.

The changes in the *bones* caused by relapsing fever were mainly a simple fattiness or reddening of the marrow. In some cases the diaphyses and epiphyses of the thigh-bones or humeri showed yellowish white infarcts of irregular spotty character and varying in size from that of a hemp seed to that of linseed. Sometimes they were discrete, sometimes united by thin bridges to coarser infiltrations.

Treatment. — I think it may be taken as pretty certain that no remedy essentially modifies the course of the disease. Relapsing fever, apparently, has its invasion, its primary five, seven, or nine days' fever, its intermission, and its relapse, in spite of all the resources of art. Some symptoms may be modified, but not apparently the great features of the disease. Thus several antiperiodics were used, without enabling me to prevent the occurrence of the relapse. The headache and arthritic pains were very severe, and though both were sometimes relieved by alkalies, it was often necessary to have recourse to opium. Colchicum seemed to have no effect on the pains. The persistent and distressing vomiting was very difficult of alleviation. Sometimes the effervescing draught, with or without hydrocyanic acid, was of service; sometimes relief was obtained by the administration of small and frequent doses of ipecacuanha, sometimes by sinapisms to the epigastrium; and in some cases all these resources were unavailing till the patient found relief in the natural issue of the disorder.

A. Rabagliati.

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F. F. W.

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